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THE PROGNOSIS FOR EPIDEMIC ENCEPHALITIS IN CHILDREN[1]

H. A. HOWE

From the Harriet Lane Home for Invalid Children, Johns Hopkins Hospital

SUMMARY

1. A series of 66 children was investigated at periods varying from 1 to 10 years after the onset of epidemic encephalitis.

2. Immediate mortality based on all hospital admissions since 1918 was found to be 11 per cent.

3. Complete incapacity was found in 19 per cent, partial incapacity in 22 per cent, and recovery in 42 per cent.

4. The acute illnesses were divided into three groups: 1. Somatic (56 per cent of the cases) characterized by paralyses or excitation of the somatic or cranial nerves. 2. Meningeal (16 per cent) in which signs of meningeal irritation predominated. 3. Abortive (19 per cent) —no true acute illness of ordinary encephalitic type, but early and frequently unheralded appearance of characteristic progressive sequelae, often accompanied by febrile reaction.

5. It was further shown that the immediate mortality was higher in the somatic group and at early ages; that recovery was almost invariable in the meningitic form, and that the most dreaded sequel, Parkinsonism, ensued most frequently after the abortive form.

6. Sequelae were divided into progressive and non-progressive, the former including hyperactivity (usually of a bizarre type), sleep inversion, personality changes, hyperpnoea, tics, etc. (all excitation phenomena), the latter characterized by residua of the acute illness in the form of paralyses, choreiform movements, emotional instability and mental retardation.

7. The non-progressive sequelae most frequently followed the general somatic type of acute illness, and, with the exception of mental retardation, offered a good prognosis.

[1] Submitted for publication March 18, 1930.

8. Progressive sequelae justified an unfavorable outlook, and, when present as initial symptoms, concomitant with the acute illness, almost invariably led to Parkinsonism.

9. Parkinsonism was further shown, as far as our series was concerned, to ensue only after a characteristic type of progressive (excitation) sequelae.

The prognosis for epidemic encephalitis in children has always been considered particularly grave. Not without cause has it been believed that, of those who escape the acute stages of the disease, an overwhelming majority falls victim to the various so-called "sequelae" in the form of mental retardation, personality changes, tics, sleep inversion, epileptiform seizures, metabolic disturbances, and worst of all, Parkinsonism. It is even maintained by some observers that any patient who recovers without complications from the acute illness could not have had true epidemic encephalitis: thus, diagnosis is made completely dependent upon the appearance of more or less serious sequelae.

The average of recovery for all forms of the disease in both adults and children is given as 25 per cent by Parsons (17) who compiled 3,558 cases over a period of ten years (through the British Ministry of Health). In 1921 Paterson and Spence (18) found the same percentage of recovery in 25 cases of epidemic encephalitis in children. This, however, represents the more hopeful side of the picture as compared with the pessimistic sketch drawn by Stevenson (21), who made careful personal studies of 65 children, many followed from 1920 until 1928. Of this number only four had made complete recoveries at the time of publication and she even states that not one had escaped absolutely scatheless from the disease.

The time element is obviously an important factor in determining whether the changes subsequent to the acute illness are for better or for worse, and the validity of generalizations regarding prognosis made in the years immediately following the first widespread recognition of the disease in 1918 may be seriously questioned. An example in point is Hohman's (11) "T. C." (No. 49—appendix) whose illness took place in 1920, whose case was described in 1921 as an illustration of typical personality changes, but who finally died in 1925, a victim of extreme Parkinsonism. In 1921 Happ and Mason (6) also described

several of the cases included in this paper. In a strikingly large number of the patients whom they reported at that time as having recovered, the most serious sequelae have ensued. Not only does the passage of time facilitate in the understanding of the metamorphosis which sequelae may undergo, but it also aids in the detection of sequelae which may appear either with or without a latent period following the acute stages of the disease. Thus the advantages of prolonged observation may be readily appreciated in the case of children who contracted encephalitis as infants. Slight but permanent intellectual damage is very difficult to establish at very early ages, yet this is precisely the period of life when such changes are most prone to take place. Unless the infant is obviously mentally deficient, one is usually forced into such descriptive phrases as "expression dull, stupid, blank, etc.," whereas when children are followed to the school age, one automatically acquires an instrument for approximating their intellectual powers.

The material which forms the basis of this paper was taken from the records of the Harriet Lane Home for Invalid Children at the Johns Hopkins Hospital, and represents all the admissions since 1918. The great majority of the children were observed in the hospital, though a few were studied through the out-patient department. Of 115 patients who were diagnosed as having had epidemic encephalitis only 66 were found suitable for this study because of difficulties in confirming the diagnosis or of tracing the children after their discharge from the hospital. Fifty were seen personally by the writer and the balance were reached by a non-technical questionnaire sent to their parents or physician. Seventy per cent of the patients were reached at least six years after their initial illness and forty-seven per cent after an interval of more than eight years.

While the diagnosis of epidemic encephalitis can frequently be made on the basis of the classical findings (more or less transient palsies or excitations involving cranial or somatic motor nerves, fever, somnolence, moderate increase in the number of mononuclear cells of the cerebro-spinal fluid), in mild cases it must frequently be a diagnosis of exclusion. It is the opinion of Parsons (17) that the mild cases are frequent, and if recognized would favorably influence the present gloomy prognosis. Considering also the fact that the severest sequelae

often follow the mild or abortive types of initial illness, a more thorough understanding of this form of the disease is imperative if any accurate prognostications are to be made. The question immediately arises whether there are any demonstrable differences between mild forms which are essentially harmless and those which later prove to be malignant.

In this series a number of borderline cases are included, but only after the rigid exclusion of many others originally bearing the diagnosis of epidemic encephalitis, but complicated by the presence of other conditions. In view of the extremely varied and numerous causes of encephalitis in infants and children, we accepted no case complicated by any evidence of tetany, lead poisoning, diarrhoea, or antecedent history of any recent infectious disease such as pneumonia, measles, chicken-pox, pertussis, vaccinia, or severe otitis media.

From the standpoint of the eventual outcome of the disease it was found profitable to classify the initial acute illnesses under three large general headings.

A. Somatic form (56 per cent of the cases): this group was characterized by affections of the general somatic and cranial nervous system. With the exception of rare hyperalgesias, the changes involved primarily the motor elements, and varied from complete, though frequently transient, paralysis and paresis to excitations evidenced by fascicular twitching, choreoathetoid movements, or general convulsive phenomena. The commonest manifestations were ocular or facial palsies, weakness and ataxia of extremities, occasional hemiplegia and paraplegias, rhythmic or random twitching of muscles of face and limbs, focal or generalized convulsions. All these phenomena were coupled with the general picture of a febrile illness. Many of the cases could be characterized by the predominance of either irritation or blockage of nerve pathways, although from the prognostic standpoint it was not found useful so to distinguish them. Somnolence, a frequent finding in this type of the disease, was also common to other forms and therefore could not be named as a characteristic feature.

B. Meningeal form (16 per cent of the cases). This type presented the picture of practically uncomplicated meningeal irritation (headache, vomiting, stiff neck, abdominal pain, positive Kernig sign, rela-

tively high mononuclear spinal fluid count). It is to be noted that the diagnosis of this type was frequently made by exclusion of other conditions which readily produce meningismus.

C. Abortive form (19 per cent of the cases). The characteristic feature of this form was the mode of onset, usually sudden overactivity with sleeplessness, often partial disorientation and hallucinations. When the children were seen soon after the acute onset, the temperature was frequently elevated (to 104°F.) and the spinal fluid cell count was increased as high as 70 mononuclears. While occasionally myoclonic movements were noted, in general there were no localizing signs, the initial acute manifestation being confined to phenomena usually considered sequelae (extreme excitement, bizarre activity, sleeplessness, etc.). Within a few days mild features of the somatic form frequently appeared (ocular or facial palsy, stupor, nystagmus). After various intervals there intervened such sequelae as tics of all varieties, respiratory difficulties, hyperpnoea, personality changes chiefly in the direction of general incorrigibility. It was never possible to isolate any definite acute illness of the usual encephalitic type: the initial attack was characterized by fever and the unheralded appearance of various progressive sequels.

Tabulation of the principal forms of the disease with outcome

TYPE OF ACUTE ILLNESS	TOTAL CASES	DEATH (ACUTE STAGE)	DEATH (FROM SEQUELS)	COMPLETE INCAPACITY	PARTIAL INCAPACITY	RECOVERY
Somatic	37	8	0	4 (10%)	9 (24%)	16 (43%)
Meningeal	11	1	0	0	1 (?)	9 (81%)
Somatic and meningeal	2	0	0	0	1	1
Abortive	13	0	3	6 (46%)	3	1 (7%)
Unclassified	3	0	0	1	1	1
Totals	66	9	3	11 (16%)	15 (22%)	28 (42%)

An examination of the accompanying table reveals several suggestive relationships. The somatic forms of the disease comprised over half of the cases and as far as complete recovery is concerned were not divergent from the general average for all types. Neither were the percentages of complete and partial incapacity far divergent from the general norm for the entire series. It will be observed, however, that the rate of recovery for the somatic form (43 per cent), as well as for

the entire series (42 per cent), is far above that usually given, the latter at best being around 25 per cent. It is true that Bing and Staehelin (3) recorded recovery in 40 per cent of their patients, but included in their series a number of cases of epidemic hiccup all of which had a favorable outcome. Of their true encephalitics only 28 per cent regained health. Obviously the favorable inclination of our figures cannot be explained solely on the supposition that our criteria for recovery were lax. In the American literature there are, to our knowledge, no figures with which ours can be fairly compared. With regard to the European statistics it seems quite definite, from our results, that among children the disease has been more malignant there than in this country, that while certain types of sequelae are prone to be as serious here as elsewhere, their incidence is lower on this side of the Atlantic.

On the other hand, the immediate mortality was 11 per cent for a series seen during the acute stages (77 cases, of which but 66 are reported since the remainder could not be traced) and in this respect does not depart from the generally accepted range of figures (7.4 per cent—Happ and Mason (6), 10 per cent—Hofstadt (9), circa 14 per cent—Stevenson (21); 15 per cent—Stern (20)). It is significant, however, that of the nine deaths at this stage of the disease, eight were attributable to the somatic form, indicating that this type was most immediately dangerous, and that once the acute illness was passed, the chance of recovery was about 44 per cent. It is also interesting to note that of these same nine fatalities, seven represented the outcome of an acute illness contracted at an average age of 20 months, and terminated in most cases within a few days' time. The two remaining deaths occurred at the ages of nine and twelve years.

The somatic group is readily seen to be a composite one and includes such forms of epidemic encephalitis as are variously classified as somnolent-ophthalmoplegic, choreiform, or paralytic with all the minor variations on the latter theme in the form myelitic, ascending bulbar, ataxic types, etc. Many authors attempt to separate one from the other, indicating a different prognosis for each, as for instance Bing and Staehelin (3) whose figures show that the choreiform type offers a relatively good prognosis from the standpoint of that most dreaded sequel, Parkinsonism, whereas the somnolent form often ends unfavor-

ably. In our series there were, perhaps, not enough cases to warrant splitting the somatic group into its component parts. At any rate, with a relatively small number in each group, there were no very apparent differences in outcome, while on the other hand, when considered as a whole, this rather heterogeneous collection presented a distinct contrast to other groups.

The meningeal group is a well recognized one, difficult of diagnosis, and generally conceded to be a relatively benign type of the disease. In our series nine out of eleven children made complete recoveries; one infant, handicapped by a severe congenital heart anomaly, succumbed, and in another child obesity, nocturnal enuresis, and questionable polyuria made its appearance five years after apparent recovery from the initial illness. Since the girl refused to come to the clinic for further study, we were unable to decide whether any connection existed between her present condition and the antecedent attack of encephalitis. It is interesting to note that while the meningeal form had an incidence of but 16 per cent, it comprised 32 per cent of the recoveries. The average time from onset until discharge from the hospital was ten days as opposed to twenty-seven days required for recovery from the somatic form.

It is the feeling among some observers that cases of this type which do not show typical sequels of encephalitis should be ruled out, and that a group which shows almost a hundred per cent of recoveries probably represents a collection of diagnostic errors. Following this line of reasoning five of the meningeal type (Nos. 39, 41, 42, 48) might be excluded from this paper, being classified as "meningismus of unknown etiology." Further purification based on the non-appearance of typical initial manifestations or sequels might be effected among two other types of cases which are included under the somatic form. (1) A group terminating in either death or complete incapacity which, without autopsy, could not with certainty be differentiated from tuberculous meningitis, brain abscess or brain tumor (Nos. 3, 17, 21, 25, 29, 31). (2) Paralytic types simulating poliomyelitis (Nos. 12, 14). The total number of patients dealt with in this paper might thus be reduced to 54, of whom 4 died in the acute stages, 3 in the chronic stages, 9 were completely incapacitated, 15 partially incapacitated, 23 recovered. It is interesting to note, however, that, according

to this interpretation, the percentages of complete incapacity and recovery remained identical (16 and 42 per cent, respectively). Partial incapacity was relatively increased (22 to 27 per cent) while the percentage of death was lowered (11 to 6 per cent). Thus, contrary to one's natural expectation the general prognosis for the entire disease became relatively more favorable.

The outcome of the abortive illness was extraordinarily bad. Out of 13 cases only one child recovered completely, one died of an acute abdominal conidtion before his fate could be determined, another was placed in the partial incapacity group on the basis of general incorrigibility. The remaining 11 children were either completely or partially incapacitated by some degree of Parkinsonism. While this form of the disease had an incidence of but 19 per cent, it accounted for 54 per cent of the complete disability. The varied manifestations of this form of the disease will be considered more completely under the discussion of sequelae.[2]

The sequelae must be considered from two different angles, first with regard to the form which they assumed, and secondly from the standpoint of the disability produced. In evaluating the extent of recovery it was found most useful to divide the patients into four groups based on various degrees of social usefulness.

(1) Death:
In the acute stages.
In chronic stages either from "recurrences" or "sequelae."

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[2] Although the total number of cases in each group is small, it should be noted that various statistically significant comparisons may be made between them (23). Thus, when the death or incapacity resulting from the abortive type of illness is compared with that caused by the remaining types, it is found that the chances of the random occurrence of this combination are but four in one thousand. Similarly in an infinite number of cases of which the recovery rate duplicated that for the general series (42 per cent), there are but three chances in a thousand that the percentage of recovery shown in the meningeal form would occur willy nilly. Chance combinations would repeat the high percentage of death due to the somatic form but three times in one hundred. When one compares the two extremes of the encephalitic picture, the number disabled by the abortive form with those who recovered from the meningeal type, the relationship is found to occur at random only once in over a thousand cases. Thanks are due Dr. L. J. Reed of the School of Hygiene and Public Health for his advice concerning these statistics.

(2) Complete incapacity:
Idiocy.
Confinement in bed because of physical incapacity (advanced Parkinsonism, etc.).
Criminal or definitely asocial conduct necessitating confinement in an institution (general incorrigibility, stealing, sexual offenses, etc.).

(3) Partial incapacity:
Mental retardation: (necessitating repetition of grades, special classes or private instruction).
Definite organic lesions with clinical signs not completely incapacitating (residual paralyses, tics, sleep disturbances, respiratory disorders, petit mal, slight Parkinsonism, speech defect).
Behavior difficulties not necessitating confinement (lying, temper tantrums, general "freshness," rather marked emotional instability).

(4) Recovery:
Clinical residuum without subjective symptoms (hyporeflexia, or hyperreflexia, sluggish or unequal pupils, slight strabismus or barely perceptible dragging of leg, etc.).
Slight subjective symptoms without clinical signs (slight feeling of awkwardness in hands, etc.).
Neither subjective symptoms, nor clinical signs.

Neurological examinations as complete as circumstances would allow were done on patients within travelling radius of Baltimore. Those who could not be seen personally were reached by means of a questionnaire.[3] Each patient was judged from the standpoint of his organic

[3] QUESTIONNAIRE: PLEASE ANSWER EACH ONE OF THE FOLLOWING QUESTIONS EITHER BY YES OR NO. IF POSSIBLE DESCRIBE EACH OF THE OUTSTANDING SYMPTOMS IN A SENTENCE.
Has the child gotten better since leaving the hospital?.....
Has the child gotten worse since leaving the hospital?.....
Is the child now perfectly well?.....Is it delicate?.....How?.....
Nervous and constantly moving?.....
Drowsy and indifferent?.....
Any difficulty in sleeping at night?.....
Overtalkative?.....When?.....
Any difficulty in talking, such as.....
voice monotonous and slow?.....
difficulty in pronouncing words?.....
willing but unable to talk?.....
does not know words?.....knows words but cannot make sentences?.....

nervous mechanism, his psychic adjustment to social conditions, and his intellectual equipment as evidenced by school records. Where there was a question of mental retardation the Binet-Simon test (Stanford Revision) was employed.

Clearly in children the most difficult factors to relate to the disease process are the psychic ones. As suggested by Neal (15), the child probably finds more difficulty than the adult in voicing his complaints, so that his psychic state must be judged very largely on the basis of behavior. Thus, probably only the grosser changes are observed. In addition one has the task of deciding whether definite behavior anomalies are the direct products of the disease itself, or only the results of subsequent indulgent and unintelligent care. Many children who have been sick for long periods are not only "nervous," but are spoiled by their families, so that we must not overemphasize in the encephalitics a degree of emotional instability which would be passed over in an ordinary child. One must also not lose sight of the fact that frequently the child discovers in his illness an effective means of getting his own way, so that the persistence of "personality changes" may simply mean that the child has found in them an effective tool for controlling his environment.

Any difficulty in using arms or legs, such as
weakness of arms.....or legs.....
trembling of arms.....or legs.....
jerking of arms.....or legs.....
stiffness of arms.....or legs.....
muscles wasted in arms.....or legs.....
arms paralysed.....leg paralysed.....
Any difficulty in controlling bladder?.....day.....night.....
Any difficulty in controlling bowels?.....day.....night.....
Is face expressionless (blank)?.....Smiles more on one side?.....
Are eyes crossed?.....Any trouble in seeing?.....
Drools saliva from mouth?.....Sweats a great deal?.....
Drinks a great deal of water?.....
Any abnormal increase in weight?.....give height and weight.....
Is breathing ever rapid and noisy?.....
Any fits or convulsions?.....Severe?.....Describe.....
During them does child fall?.....become unconscious?.....
.....

In grouping the cases with regard to degree of social recovery, it became apparent that most of the disability resulted from two widely different types of sequelae, mental retardation and Parkinsonism. This circumstance led to a classification of the actual sequelae themselves as progressive and non-progressive. The former have already been touched upon in the discussion of the abortive form of acute illness. It is this group which is responsible for the terror which attaches to the name encephalitis: it comprises such manifestations as the wild hyperactivity which yields to no treatment, the stubborn inversion of sleep rhythm, bizarre tics, distressing respiratory spasms, puffing, blowing, spitting, drooling, etc. Also in this group are included the anomalies expressed in asocial conduct (lying, stealing, sexual aggressiveness, general incorrigibility) and, lastly Parkinsonism. With the exception of this final manifestation all these varied forms represent excitation phenomena (Leyser (14), Sherman and Beverly (19), Bond and Partridge (4), Fleck (5), *et al.*). It was the implication of our cases that these diverse sequelae in the end all tended to con-

---

Is child able to look after his own wants?.....
Understands everything that is said?.....
Mentally slow?.....
Any change of personality or disposition, such as

cross?.....	likes to be alone?.....
cruel?.....	runs away?.....
temper tantrums?.....	indifferent to everything?.....
lies?.....	fearful?.....
steals?.....	hears imaginary voices?.....
hard to manage?.....	sees things?.....
highly sexed?.....	always gets his own way?.....
masturbates?.....	memory poor?.....

If there has been any change of disposition please describe what child used to be like.....
.....
Any peculiar habits of holding mouth open, spitting, clearing throat, making queer movements with hands, etc. Describe.....
.....
Does child go to school?..... In what grade?.....
Any difficulty in school?..... Any grades failed?.....
Remarks:.....
.....

verge at one common point, Parkinsonism. Though all were apparently manifestations of a similar process, the most serious single sequel was the extreme overactivity which was present as an early symptom in every case of the abortive form, one case of the somatic form (22) and one of the meningeal (46). With two exceptions (one meningeal (46) and one abortive (59)) every child developed some features of Parkinsonism. There were no other cases of outspoken Parkinsonism. In two other cases (somatic) where one isolated excitation phenomenon (tachypnoea) was present early in the disease, one patient developed some transient Parkinsonism feature (mask face and stiffness of limbs).

On the basis of our findings, it appears that Parkinsonism is the final stage of a series of phenomena usually considered sequelae, which ensue most frequently in connection with the abortive form of the disease, and are characterized primarily by excitation. Parkinsonism need not inevitably follow this train of events, since recovery occasionally takes place, but its incidence is exceedingly high where these sequelae appear early in the disease. The onset of the syndrome seems to differ from that in adults in being less insidious and more often preceded by definite encephalitic manifestations. The journals are filled with numerous examples of the late development of such sequels as sleep inversion, tics and personality changes. In our series these phenomena appeared in only three patients who had not shown as an early symptom marked overactivity or some similar type of excitation previously described. These children subsequently recovered without any signs of Parkinsonism.

There is a considerable body of literature concerning Parkinsonism in children. Bing and Staehelin (3) did not find it ensuing after the choreiform and spinal types of encephalitis, but record a high incidence after their lethargic form. Bond and Partridge (4), after a year's observation of 17 children admitted for behavior disturbances, concluded that these were not progressive and saw no signs of Parkinsonism. Judging from their rather brief medical histories, the cases seemed to be light forms of what we have called the somatic and abortive types of the disease. Although the lightness of the initial attack may have had some connection with the relative favorability of the outcome, the question can be finally settled only by the passage

of time. Hofstadt (10) was unable to correlate the appearance of Parkinsonism with any form of the disease, although it is interesting that of eight cases of this syndrome cited in detail, six showed previous excitation in the form of sleep disturbances. Stevenson (21) reports that she was unable to find any relation between the early history and the appearance of Parkinsonism. She cites 22 cases of this syndrome in some detail, but does not call attention to the fact that 20 of them previously showed the type of malignant excitation characterized by nocturnal restlessness, overactivity, hyperpnoea, bad conduct, etc.

Fleck (5) has described 42 cases of encephalitic behavior anomalies most of which he characterized as being hyperexcitable. At the date of writing, 52 per cent had developed Parkinsonism, and although 38 per cent showed some improvement in their behavior, 62 per cent of them purchased it at the cost of advancing Parkinsonism. A similar observation has been made by Herd (7). Kwint (13), who studied 42 chronic cases admitted to Der Ukrainische Staatliche Psychoneurologische Institut at Crakow, found disturbances of sleep in 38, with hyperactivity in the majority of these. Parkinsonism had developed in but 12 children (8 of whom had previously shown hyperactivity). The cases, however, were of too short duration to indicate the real incidence of this syndrome. The percentage of Parkinsonism is variously given by different authors (Werner (22), 69 per cent; Hofstadt (10), 60 per cent; Fleck (5), 52 per cent; Auden (2), 43 per cent; Kennedy (12), 35 per cent; Stevenson (21), 30 per cent; Kwint (13), 28 per cent). In our series it was found in but 19 per cent of the cases (13 children, 5 of whom showed only one or two features, Nos. 49, 50, 52, 53, 54, 55, 56, 57—11, 22, 58, 60, 61).

There are two possible explanations for this discrepancy, the first being that some of the observers cited above saw a larger percentage of chronic cases, which would naturally be more prone to this sequel, and second, that there were geographical variations in the types of the disease. This latter possibility is borne out by the cases of the Royal Hospital at Glasgow which were collected in 1922 and 1928 by Anderson and Stevenson, respectively. The first compilation described 65 per cent of the children as suffering from sleep inversion, while but one in forty had developed Parkinsonism. Six years later in a careful review of supposedly some of the same cases, Anderson found noctur-

nal excitement in 61 out of 73, while the number of Parkinsons had grown to 30 per cent. Thus the connection between these two sequelae is not merely accidental, and is further accentuated by the passage of time. When one considers that the incidence of these progressive excitor sequelae was but 22 per cent in our series, it is not surprising to find the Parkinsons hovering around 19 per cent.

While the geographical variations in the type and severity of the acute illness have already been pointed out, the fluctuations from year to year have also been of interest. In Europe the epidemic of 1920 was regarded as a very serious one from the standpoint of Parkinsonism (Hoff (8) *et al.*). Similarly our series shows a high incidence of the abortive form in that year, while all of the serious Parkinsons were stricken at that time. The year 1920 saw 38 per cent of all the cases included in this paper (25), and accounts for 57 per cent of the disability.

There is another variety of sequel of epidemic encephalitis which is never progressive and tends to become milder with the passage of time. This type probably represents immediate damage to the nervous system during the acute stages of the disease, and persists for a variable interval after the subsidence of florid symptoms. In this group we include paralyses, choreiform movements originating during the acute stages, general emotional instability, and mental retardation. With the exception of the last finding, which may become less apparent with the passage of time but never disappears, all these forms offer a good prognosis. Emotional instability (shown by temper tantrums, fearfulness, boisterousness, low threshold of excitability, night terrors, enuresis, etc.) was a common finding after uncomplicated somatic forms of the disease (15 instances) and in 6 cases has persisted until the present writing. In several cases mothers reported that the children yelled, screamed, were fearful and almost unmanageable for variable periods up to 18 months, but were subsequently found in good health. Though none of the children were seen during the acute stages, we nevertheless feel that there was probably an actual qualitative difference between this type of benign instability and the malignant hyperexcitability which made its appearance early in the disease. The former was *never* seen as an initial symptom, and was hardly more than an accentuation of the traits usually found in spoiled children.

There was also little indication of a behavior picture resembling the maniacal, lawless overactivity of the progressive form (bumping head, tearing sheets, decorating feces, attacking patients, etc.); neither were the children described as "fresh," a word frequently applied to milder degrees of the progressive excitation.

This distinction is advanced with considerable hesitation. Although the case histories utilized in this paper represent as accurate a portrayal of the facts as could be expected from the efforts of many individuals extended over a period of several years, they are not concerned primarily with the intricacies of behavior. It is therefore, perhaps, pushing the analysis too far to draw any conclusions based on such fine points. Obviously, in many cases it would be exceedingly difficult to differentiate between these two types of excitement. In such instances it is the *early* appearance during the acute illness of such excitation phenomena as overactivity, sleeplessness, bizarre behavior, or hyperpnoea which must be regarded as an extremely unfavorable sign.

Motor nerve paralyses tended to clear up, though occasionally they left slight residua in the form of almost imperceptible weakness of face or limbs, hyperreflexia, slight subjective clumsiness, with rarely enough pyramidal tract involvement to give ankle clonus or positive Babinski. In many cases these evidences of the disease were no more incompatible with recovery than would be the scar from an operation. Choreiform movements were present during the acute illness in 15 patients and persisted in two (Nos. 26 and 31). Convulsions were noted in 22 cases and were found at present writing confined to two (Nos. 17 and 34). One child has had almost continual incontinence of urine for over three years following his illness.

The only children who were reduced by the disease to complete idiocy were stricken at the ages of 5 weeks, 11 months, 15 months, 3 years, respectively, (average age 15 months) while those who showed definite signs of mental retardation became ill at 4 months, 16 months, 3 years, 3.2 years, 3.5 years, 4 years, 7 years (average age, 38 months). This in general bears out the dictum that it is the young children who suffer intellectual damage, but does not indicate that they are invariably so affected: of all the children five years or under, 42 per cent made complete recoveries at an average age of 33 months.

Of somewhat ambiguous position in our classification of sequelae

are a questionable metabolic syndrome (No. 38) showing adiposity and nocturnal enuresis after a five-year latent period, and four cases characterized by convulsive seizures of variable frequency. It is doubtful whether the former had any connection with encephalitis. Of the four epileptoid patients, one child (No. 43) developed attacks after an indefinite latent period and recovered several years later. The remaining three children (Nos. 6, 17 and 34) suffered from epileptiform seizures which may be regarded as a continuation of their acute illnesses in which convulsions had been a prominent feature. One (No. 6) recovered 21 months after the onset; the two remaining have had the attacks for three and eight years, respectively; both are idiots, unable to talk or look out for themselves in any way.

As already noted, 9 out of 77 patients died in the acute stages of the disease, one with apparently a florid febrile exacerbation of convulsive seizures two years after an initial illness in which convulsions were the most striking manifestation. This case, however, in the absence of an autopsy, could not surely be distinguished from one of brain tumor. There was one death from an acute abdominal condition, and two fatalities from intercurrent infection among the ranks of the Parkinsons.

With regard to several of the children who contracted the disease during the last three years, it is possibly too early to say whether their recoveries have been complete. Two of these are still below the school age and may subsequently show signs of mental retardation. Of the four children who made complete recoveries in spite of some involvement by "progressive sequelae," all now seem to be completely out of danger of Parkinsonism.

In the partial incapacity group there are fifteen patients, of whom ten can never attain complete restitution since they suffer from variable degrees of intellectual defects. The remaining 5 children whose troubles are neurological, behavioristic or metabolic give some indication that they may recover.

Only the complete incapacity group is an absolutely hopeless one. It is composed entirely of Parkinsons and idiots (respectively 12 and 7 per cent of the total cases). Of these, two have already died and one can look forward to nothing better for the others.[4]

[4]The writer wishes to express his gratitude to Dr. Edwards A. Park of the Department of Pediatrics for his criticism and encouragement.

Somatic

1. 19355. B. R., aged 2 yrs. White female. Onset 10–2–18: weakness, restlessness, jerking of face, arms and legs, nystagmus, left facial weakness, flexibilitas cerea, T. 100°, 92 cells. Discharged 10–21–18, improved but with facial weakness. For one year yelled, screamed, completely unmanageable. Had to be retaught to walk and talk. 3–14–29, no complaints—pupils large and sluggish, slight residuum of left facial weakness. Recovery.
2. 16167. P. W., aged 2 yrs. Colored female; mother treated for syphilis 8 mos. before delivery, child normal, blood and spinal fluid Wassermann negative. Onset 1–27–19: T. 99.4°, stupor, weakness and coarse tremors of head and extremities, unable to walk, slight internal strabismus and left facial weakness, flexibilitas cerea. Discharged 3–6–19, improved but unable to walk. 5–15–19, walks well. Until 1921 a frequent dispensary visitor for bronchitis, tonsilitis, cough, enuresis—no obvious sequelae of encephalitis noted. Not traced after 1921.
3. 20849. M. H., aged 7 wks. White female. Onset 4–1–19: deep stupor (takes food), transient ptosis, slight left facial weakness, becomes spastic on stimulation, slight *tache cérébrale*, T. 101.6°, 28 lymphocytes, Pandy slightly plus. Haemolytic streptococcus cultured from throat. Discharged 4–16–19, improved, but still very stuporous. 5–8–19, slightly more lively. 6–7–19, suddenly worse—death—details not available.
4. 22028. E. R., aged 3 yrs., 6 mos. White female. Onset 7–13–19: comatose, clonic convulsions almost continuous, starting left and became general, int. strabismus and nystagmus during convulsions, bilateral ankle clonus during convulsions, T. 105.5°, 96 mononuclears, Pandy sl. plus, fine film. Discharged 8–18–19, normal. 2–25–29, no complaints, complete recovery. (Report from parents, not personally seen)
5. 22490. C. S., aged 2 yrs. White female. Onset 8–25–19: T. 103°, stuporous, internal strabismus, trembling of left eyelid and watering of left eye, weakness of legs, 30 cells, Pandy 0, Wassermann not done. Discharged 9–6–19, recovered. 4–2–29, no complaints, scarcely perceptible weakness of left leg with suggestion of Babinski and Oppenheim (produce no subjective difficulty). Recovery.
6. 27600. V. L., aged 3 yrs. White female. Onset 9–?–19: "flu;" slept 2 weeks general convulsions, left face paralysed, left leg practically paralysed, left arm weak. 10–?–19, attacks simulating petit mal q.d. 12–?–19, paralysis gone, attacks continue with gradually decreasing frequency until 6–11–21 (T & A) after which only two, sleep inversion until operation; very fearful. 3–28–29, no complaints, reflexes sluggish on left, slight lag of left face, slight incoördination of left hand (finger-nose test). Recovery.
7. 24198. F. M., aged 8 yrs. White male. Onset 1–17–20: T. 97.6°, vomiting, diplopia, rt. facial paralysis, hearing in rt. ear impaired, 8 cells, Pandy 0. Discharged 2–13–20, improved but still with facial weakness. 3–28–20,

brought to psychiatric clinic for twitching eyes, rolling of tongue, staring, quarrelsomeness, petty stealing and lying; home situation considered bad. Binet-Simon 8 yrs., 10 mos. 3–2–21, facial weakness gone, in fine condition. 1–5–29, has been in various boarding homes since 1921, has made good adaptation to rather trying situations in these homes, considered college material by his high school teacher. How much of the behavior disorder was on an organic and how much on a situational basis cannot be decided. At any rate recovery is complete. Not seen.

8. 25157. M. B., aged 3 yrs., 5 mos. White female. Onset Feb. 1920; periodic diurnal somnolence for 3 months followed by mild sleep inversion, weakness of neck, arms, legs, tremor in arms of intention type, T. 99°, 3 cells, Pandy 0. Admitted 6–12–20; discharged 6–15–20, limbs stronger. Sleep inversion persisted 18 months. 3–9–29, general health fairly good, slightly obese, marked speech defect, neurological neg., does poorly in school, will probably fail this year, chronological age 12 years, 2 months, mental age 10 years, 8 months. Partial incapacity.
9. 14553. P. K., 13 yrs. White male. Onset 2–8–20: T. 100.2°, slurring speech, left facial weakness, ataxia of arms more on left, left leg dragged, ankle clonus more on left, incontinence of urine and feces, obstinate constipation, 1 cell, Pandy 0. Discharged 3–1–20, without apparent sequelae. 8–20–20, irritable, sent in for enuresis which he had prior to illness. 4–1–29, now 22 yrs. old, enuresis persisted until 3 yrs. ago, a tall, thin, underdeveloped man, no complaints except nervousness and irritability, reflexes of arm and leg very slightly more active on left, slight weakness of extensors of left arm. Recovery.
10. 24437. A. W., aged 5 wks. White male. Onset 3–15–20: illness began as "pneumonia" with T. 102°, dyspnoea, cough; slight improvement followed in two weeks by convulsions (athetoid movements of extremities, dyspnoea, cyanosis) lq. d. Admitted 4–6–20, transitory ptosis of right lid, general spasticity, marked tachypnoea, 34 cells, mostly mononuclears, Pandy plus. 4–20–20, discharged improved. A frequent visitor to out-patient dept. for regulation of feeding. 4–20–22, now 2 years, 5 months old, neither walks nor talks, impulsive, overactive, silly grinning, must be wrapped in blanket to be fed. No careful note regarding possible Parkinsonian features. Complete incapacity.
11. 24259. A. Y., aged 4 mos. White female. Onset sudden 3–17–20: convulsions (generalized), stupor, opisthotonos, stiff neck, internal strabismus, right facial weakness, marked tachypnoea (92), no abdominal reflexes, 10 cells, Pandy 0, T. 103°, tachypnoea persists until 4–14–20. Discharged 4–28–20, with only internal strabismus persistent. 1–18–21, "crying spasms," rickets, chronic otitis. 10–19–22, seen by social worker, thin, pale, walks stiff-legged, speech difficult to understand. 1–3–29, mother reports that for several years following illness patient cried and whined continually, tore up sheets, clothing, etc. Could not run and jump until 5 years old.

Is still nervous, always picking at things, cannot keep quiet, confabulates, steals small articles, has been in special class for backward children for 2 years, attention fleeting and memory poor. Present age 10 years, expression very often blank, and eyes staring, requests must frequently be repeated, often lapses into complete inattention, mood a rather shallow euphoria, coarse tremors of hands, nails bitten to quick, pupils almost fixed, slight left internal stabismus more marked on fatigue, inability to converge, K. K. slightly more active on left, slight incoördination left, in heel-knee test, drags left leg almost imperceptibly. Has shown marked improvement in last five years but is still in partial incapacity group.

12. 25691. F. S., aged 10 yrs. White female. Onset insidious, May 1920. Question between polyneuritic form of epidemic encephalitis and poliomyelitis. Admitted 7–30–20, weakness of legs and arms, moderate reaction of degeneration in leg muscles, absent knee and ankle jerks, pupils sluggish, blurring of nerve heads on nasal side (esp. rt.), aching of legs, nausea, vomiting, frontal headache, tired feeling, 28 mononuclears, Pandy plus, colloidal gold curve 2233554100, T. 99°. Discharged 8–19–20, much stronger, but still without leg reflexes. April 1929, questionnaire returned by patient herself, now 19 years old. No complaints, graduated from high school in 1928, with exception of "nervousness" which she had always had, and a vague "nervous attack" four years after leaving the hospital, has been in perfect health. Writes that she has never been in better health, but is nevertheless planning to come to the hospital for examination. No sequelae. Recovery.
13. 25296. H. B., aged 8 yrs. White female. Onset 5–17–20: T. 101°, stupor, dysphagia, dysarthria, double internal strabismus, choked discs, weakness and ataxia of rt. arm and leg, rt. facial weakness, rt. arm finally paralysed, 9 cells, Pandy 0, developed some râles, more stuporous, died of respiratory failure.
14. 26322. R. G., aged 1 yr. 5 mos. Question between poliomyelitis and encephalitis, white female. Onset 9–17–20: irritable, projectile vomiting, T. 103°, flaccid paralysis of rt. leg, 4 hrs. later becoming spastic; relaxation and twitching during sleep. Child cries with pain when legs are extended or is made to stand. Discharged 10–2–20, able to walk. 4–1–29, relative who is physician reports that patient has no sequelae whatever, either mental or physical. Recovery.
15. 26244. W. B., aged 1 yr. 8 mos. White male. Onset 9–20–20: T. 98.8°, stuporous, nystagmoid movements of eyes, internal strabismus, twitching of face, rigidity of jaw muscles, Chvostek pos., no A. J., 8 mononuclears, Pandy plus. Discharged 9–25–20, improved but with internal squint. 2–23–21, reported normal by mother. April 1929, questionnaire, no complaints, indistinguishable from twin sister who did not have the disease. Recovery.
16. 27443. J. K., aged 5 yrs. White female. Onset insidious Dec. 1920. Admitted 1–24–21, right facial weakness, left arm and leg weak, athetoid

movements and fascicular muscle twitching, hearing impaired, unable to walk, period of deep stupor for a week followed by a month of violent hyperactivity, improved by intercurrent infection. Discharged 5–22–21, quieter and without weakness, but not talking. 2–23–29, patient 14 years old, only complaint is weakness of ankles and swelling of feet after walking, reported to have been nervous and irritable for two years following illness, but is of quiet, even disposition now, very slight speech defect. Recovery.

17. 27172. A. G., aged 1 yr. 3 mos. White female. Onset 12–14–20: T. 100°, 25 to 30 tonic convulsions per day, left internal strabismus, choreiform movements, 7 cells, Pandy 0. Discharged 1–8–21, convulsions controlled by luminal. 7–6–22, spells of several convulsions every 2 or 3 months, has never talked or played, wears diapers continually, very difficult to control. 3–7–29, has been in mental hospital for two years, because she could not be managed at home. Does not talk or recognize people, no sense of danger, violent temper. Series of convulsions every few months, some causing loss of consciousness. No apparent physical disorders. Idiot—complete incapacity.
18. 27283. I. H., aged 13 yrs. White female. Onset 12–12–20: vomiting, T. 102°, inability to talk, transient rt. hemiplegia, convulsions (generalized and rt. side), choreiform movements of rt. arm, flexibilitas cerea more on rt., left facial weakness, beginning choked discs more on rt., 6 cells, Pandy faintly plus. Cranium opened for brain tumor without positive findings. Discharged Apr. 1921, much improved, though did not recognize family. Had to be taught to talk and count, but regained entire vocabulary in a few weeks. For months emotionally unstable, alternating between affection and cruelty, temper tantrums, difficulty in swallowing. 4–16–29, patient now 21 yrs. old. No complaints except nervous indigestion. Is employed as a secretary. One year ago had generalized convulsion during which she became unconscious. This was like the ones which occurred during her illness only less severe. Gives no evidence of illness except slight emotional instability, hyperreflexia of rt. arm and some subjective stiffness in rt. hand noticed in playing the piano. Recovery.
19. 28298. M. B., aged 7 yrs. Colored female, always delicate. Onset 4–10–21: frontal headache, pain in legs and arms, head and eyes turned to right, pupils small and fixed to light, constant flinging of left arm, slight flattening of nasolabial fold, left, T. 98°, 8 cells, Pandy 4+. Colloidal gold curve 001332100, Wassermann 0. Discharged 5–24–21, completely recovered after having been through a short period of boisterousness following the lifting of the coma. 3–16–29, present age 15 years, tall thin mulatto girl, only complaint irregular menstruation and pain in l.l.q. before flow. Has temper and crying spells followed by headache for which she receives considerable solicitude; whole family (parents and 7 children) emotionally unstable, but patient is the worst. Neurological examination negative except

for slight weakness and cogwheel resistance in left leg, patient says this leg trembles when she is excited. Exceedingly brilliant in school, plans to be teacher. Although some sequelae are present, they are not considered severe enough to bar her from the recovery class.

20. 29409. W. H., aged 2 yrs. White male. Onset sudden 6–26–21: generalized convulsions as many as 25 per day, unsteady slapping gait, ataxia of arms and legs, partial paralysis of left arm and leg, left facial weakness, positive Babinski rt., bilateral ankle clonus, absence of abdominal and cremasteric reflexes, great irritability, T. 99°, diagnosis of cerebellar tumor unconfirmed by trephine. Discharged 7–25–21, unimproved. Readmitted 8–30–21, with essentially the same picture, now unable to stand or sit unsupported. Discharged 9–20–21 improved, but still very ataxic. 3–27–29, questionnaire, after discharge from the hospital convulsions were controlled with luminal; none after 10–19–21. For a year and half after illness great emotional instability, took violent dislike to sister whom he formerly loved, screamed and cried when she or any other child came into the room. Until recently has been subject to attacks of "acidosis." At present is "high strung" and subject to respiratory infections. Paralyses and ataxia entirely gone. Leads class at school. Plays piano and violin. Present age 9 yrs. Recovery.
21. 29755. R. T., aged 9 mos. White male. Onset 8–20–21: generalized convulsions, no spontaneous movements of rt. extremities, rt. sided convulsions, nystagmoid movements of eyes to rt. during convulsions, rt. triceps reflex lost, biceps sluggish rt., stupor, T. 104°, 16 cells 50% mononuclears. Discharged 9–5–21, much improved but still not using rt. arm. 1–6–22, pharyngitis, otitis, bronchopneumonia, still has weakness and spasticity of rt. arm and leg. Has had 3 unheralded convulsions in last 4 months, beginning rt. and becoming general, followed by sleep. 8–20–23, readmitted for convulsions, beginning left and becoming general, rt. side apparently paralysed, feeble rt. Died before further tests could be made. No autopsy.
22. 30097. D. R., aged 4 yrs. White female. Onset 9–17–21: vomiting, moment of unconsciousness, delirium, restlessness, screaming, eyes staring, and deviated to left, pupils sluggish, slight weakness of rt. arm and leg with ataxia of same, does not talk, T. 98.8°, 12 cells, Pandy plus, vaginal smear shows gram-neg. diplococci. Discharged 12–15–21, improved but not normal, now able to speak. 11–23–23, seen in psychiatric clinic for speech training (has always had slight speech defect which was accentuated by illness), rather expressionless face, reptilian eyes, slow movements, loss of associated movements, mental age 7 yrs. 3–2–29, aged 11 yrs., 9 mos., slow, rather apathetic, face blank until child smiles, talks in faint sing-song voice, slight speech defect, all reactions slow, now in 4th grade which she is repeating. Binet-Simon test gives mental age of 10 yrs., chron. age 12 yrs. Attention fleeting. Spares right leg in walking, slight weakness and ataxia of rt. leg, questionable Babinski rt., bilateral ankle clonus, left abdominal reflex

not obtained, pupils large, react to light, but not to accommodation, convergence poor. Partial incapacity.

23. 30184. W. J., aged 2 yrs. White male. Onset 10–5–21: vomiting, generalized convulsions, stupor, slow involuntary rhythmic movements of extremities initiated by outside stimuli, as stupor deepens into coma the movements cease. T. 102.8, 6 cells, Pandy 0. Discharged 10–11–21, normal. 4–17–23, returns for scabies, no sequelae noted. Not followed further. Recovery.
24. 31706. W. S., aged 7 yrs. White male. Onset 1–15–22: partial paralysis rt. face, spastic partial paralysis of arms and legs more marked on rt. Reflexes hyperactive, bilateral Babinski (process began with left hemiplegia) tinnitus and hearing defect (left), gross ataxia of extremities, dysarthria, dysphagia, choked disc more on rt., projectile vomiting, T. 98.6°, 4 mononuclears, Pandy plus. Discharged 3–22–22, improved. 10–2–22, letter from father reports rapid improvement. Runs and plays, though left arm and leg are still "slightly stiff," nervous. 3–21–29, questionnaire, still has weakness and stiffness of arm and legs, (bilateral?). Enuresis until last year. Now 14 yrs. old and growing rapidly, mentally slow, now in second grade, comprehension and memory poor, though there has been great improvement in the last two years Partial incapacity.
25. 30995. E. M., aged 1 yr., 8 mos. White male. Onset 1–17–22: question between tuberculous meningitis and encephalitis, transient paralysis left face, rt. arm and leg, generalized convulsions, "pumping" movements of extremities, coma, pupils dilated, general spasticity, positive Babinski and ankle clonus rt. T. 99° on admission (1–13–22), lumbar punctures bloody, congenital heart malformation also present. 1–16–22, lateral nystagmus, rt. internal strabismus, T. 109°, died of respiratory failure,
26. 32721. W. C., aged 16 mos. White male: Onset 5–12–22: vomiting, convulsions and continual choreiform movements of head and extremities, coma, T. 104°, ankle jerks, K.K., and abdominal reflexes not obtained, 2 mononuclears, Pandy faintly plus, admitted 6–22–22 for diagnosis. Dis charged 6–23–22 unimproved. March 1929, questionnaire, child has improved greatly but still has choreiform movements of rt. arm and leg. When walking, holds rt. hand out with fingers stiffly extended. Present age 8 yrs. Taught at home. Visual memory described as poor, auditory memory good, many things child does not grasp, temper tantrums, sometimes runs away, sometimes fearful, hard to manage. Partial incapacity.
27. 32742. N. D., aged 3 yrs. White female. Onset cannot be definitely dated. Vague spells of weakness, slept most of time for several days. 6–10–22, rt. eye turned in for a week, vomiting, did not talk, difficulty in walking, seen only in dispensary. 6–24–22, speech thick, pain in leg, KK not obtained. T. 98.8°, tonsils enlarged and injected, looks well. 6–24–22, T. 100.4°, sleeps better, speech better, headache. 7–13–22, walks and talks better. 3–2–29, described as "nervous," temper tantrums, the most difficult of 11 children

from disciplinary standpoint. Has failed 2 grades at school, age 9 yrs. Binet-Simon gives mental age 9 yrs. (possibility of defective vision being accountable for scholastic deficiency), speech slurring, child says T for D, greatly hypertrophied tonsils and adenoids, neurological examination neg. Placed in partial incapacity group on basis of emotional instability and speech defect.

28. 34043. H. H., aged 3 yrs. White female. Onset 10–4–22: drowsiness, irritability, left facial paralysis, left pupil larger, paralysis of internal rectus muscle left, external rectus rt., transient spasticity of extremities, T. 99.6°, 38 mononuclears, Pandy plus, incontinence of urine and feces. Discharged 12–13–22, with only internal strabismus. 6–2–24, in fine physical condition, sl. residuum of facial paralysis, internal strabismus; reported to be less alert mentally than before illness. 3–13–29, present age 10 yrs. Started school at 6 yrs., now in third grade with no possibility of advancing this year, cannot read or remember words which have been repeatedly told her. Binet-Simon gives mental age of 8 yrs., 3 mos. Child is indifferent to her defect, not interested in school, is excitable, easily frightened, sleep easily disturbed, bites finger-nails, eyes cannot be turned to rt., facial weakness lower left, slight weakness and dragging of left leg, Babinski, ankle clonus, hyperactive KK left (not obtained on subsequent examination one week later). Partial incapacity.
29. 34532. C. W., aged 1 yr., 5 mos. White male. Question between brain abscess and encephalitis. Onset 12–11–22: vomiting, sl. rigidity of neck, and rt. knee, tremor of hands and weakness of rt. arm, constant purposeless movements of left arm, suggestive ankle clonus. T. 102.5°, 7 cells, Pandy 0, coarse râles over both lungs, respiration becomes more labored, death 12–25–22 from respiratory failure. No autopsy.
30. 38060. D. W., aged 2 yrs., 7 mos. White female. Onset 10–7–23: drowsiness, rt. facial paralysis, lacrimation of rt. eye, difficulty in chewing, rt. internal strabismus, rt. pupil large and sluggish, slight but definite atrophy of discs, dragging of rt. leg, athetoid movements of arms, ataxia of all extremities, positive Brudzinski sign, T. 98.6°, 5 mononuclears, Pandy 0. Discharged 10–29–23, much improved, able to stand but unsteady. 12–?–23, no difficulty in walking, no facial paralysis, rt. eye still turned in. 3–30–29, age 8 yrs., easily excited, trembles all over, cannot recite when called upon in school, school record good, bites finger-nails, afraid of dark, rt. eye waters when child strains at stool. General health good. Neurological exam. neg. except for slight rt. internal strabismus, KK slightly more active rt. Partial incapacity on basis of emotional instability.
31. 39320. E. F., aged 11 mos. White male. Onset November, 1923, fever, generalized convulsions, head retracted, neck stiff, since acute onset until admission (2–16–24), continuous movements of head and extremities, fed two months by gavage, hyperaesthesia, T. 99°–101°, 10 cells, Pandy tr. Dis-

charged 2–22–24, unimproved. March, 1929, questionnaire. Now 6 yrs. old, still has jerks, choreiform movements of arms and legs, left leg paralysed, and atrophic, unable to talk though he seems to try, sucks thumb, mouth held open, drooling, does not understand what is said to him, cannot look after his own wants, often fearful, runs away, memory poor, does not go to school. Complete incapacity.

32. 38841. K. K., age 1 yr., 1 mo. White female. Onset 1–2–24: generalized convulsions, left internal strabismus, left facial weakness (pupils dilated and fixed to light just after convulsions), spasticity of extremities, coma, T. 104.6°, 17 cells, Pandy ?. 1–8–24, T. 108°, many convulsions, death. Duration of florid stage of disease 3 days. Autopsy revealed enlarged mesenteric lymph nodes, collections of periportal fat in liver, no lesions found in brain. The pathological department did not consider this incompatible with the diagnosis of epidemic encephalitis.
33. 40426. D. E., aged 1 yr., 8 mos. White female. Onset 5–5–24: alternation between coma and overactivity, twitching of rt. face, paralysis of rt. arm, weakness of rt. leg, aimless thrashing movements of extremities (except rt. arm), exanthematous rash over abdomen, T. 106°, 13 cells, Pandy plus. On several occasions respiration ceased and child was revived by artificial respiration. T. rose to 108° day before child died of respiratory failure, 6–5–24. No autopsy.
34. 44451. J. B., aged 3 yrs. Colored female. Onset 5–2–25: drowsiness, delirium, convulsions, vomiting, left facial paralysis, left leg weak, myoclonic movements, sphincter incontinence, T. 104°, 2 cells, Pandy 0, Discharged 5–16–25 much improved, facial paralysis gone, but very dull mentally. 10–23–25, active but unresponsive, knows only two words, cheerful, still incontinent. 2–25–29, child 7 yrs. old, idiot, cannot be left alone, no sense of danger, knows only a few words, cannot form sentences, marked speech defect, obeys only the simplest demands, 2–3 epileptiform attacks per day, covered with scars and burns from falling on stove, floor, furniture, etc. No neurological changes made out though complete examination was impossible because of lack of coöperation. Complete incapacity.
35. 48104. K. G., aged 13 yrs. White female. Onset 2–11–26: severe headache, epigastric pain, hyperaesthesia of left middle finger, bilateral internal strabismus and ptosis, right disc slightly blurred, left disc obscured by corneal ulcer, extremities spastic, marked dermatographia, reflexes hyperactive, later sluggish, positive Kernig, neck stiff, coma, T. 105°, 3 cells, Pandy 0, gradual deepening of coma, and slowing of respirations, with death from respiratory failure 3–4–26. Diagnosis confirmed by autopsy findings.
36. 53835. W. M., aged 3 yrs., 3 mos. White male. Onset 1–?–27: headache, convulsions, stupor, twitching of rt. arm, blindness, vertical nystagmus, blurring of disc. T. 102°, 5 cells. Seen for diagnosis 6 mos. after acute illness (7–11–27). Pupils dilated and sluggish, low grade secondary optic atrophy,

neurological neg., irritable and spoiled. March, 1929, questionnaire from parents and from family physician; constriction of visual fields, irritable and cruel (probably accounted for on environmental basis), question of mental retardation, child 5 yrs., 5 mos. old and has not been to school; case tentatively placed in partial incapacity group. It is not possible to place him definitely after only two years.

37. 54112. M. Z., age 4 yrs. White female. Onset 8–1–27: headache, projectile vomiting, clonic and tonic convulsions with opisthotonos, carpopedal spasm, pupils dilated, transient rt. internal strabismus, left facial weakness, abdominal reflexes not obtained, transient bilateral Babinski, deep stupor, T. 97°, 85 mononuclears, Pandy 0. Discharged 8–6–27 against advice, no longer drowsy, no paralysis or weakness, mask-like face. 8–30–27, no complaints, eats and sleeps well. 3–29–29, child not seen, mother uncoöperative. Now 5 yrs., 5 mos. old, no complaints, except frequent gastro-intestinal upsets which were present before illness. Child is healthier than ever before. Bright and active, no weakness of face or extremities observed by mother. Has not started to school but can write her name. Recovery.

Meningeal

38. 12119. H. C., aged 7 yrs. White female. Onset 10–10–20: T. 102°, drowsiness, vomiting, tender neck, headache, photophobia, *tache cérébrale*, questionable left facial weakness, positive Kernig, bilat., 60 mononuclears, Pandy plus. Discharged 10–14–20, completely recovered. 12–27–20, no sequelae. April 1929: last 3 years has become increasingly obese, Ht. 5′ 4″, Wt. 170 pounds, has at same time developed enuresis, quantity of urine is not strikingly increased, but patient voids rather frequently during day, drinks a good deal of water, occasional frontal headache, spells of vertigo, menstruation regular and normal, neurological examination negative, eye-grounds normal, no visual difficulties, no change of disposition, no school difficulty, started at 6, now 13 years 9 months old, and in the 8th grade. Patient unwilling to come to hospital for further study so that at present it is impossible to decide what factors underlie these changes of the past 3 years. Though a latent period of 5 years has intervened since the acute illness, it is possible that the condition represents a sequel of encephalitis.

39. 27374. R. A., age, 8 yrs. White female. Onset sudden, 2–2–21: vomiting, abdominal pain, headache, T. 102°, stupor, jerking of legs and rt. arm, choked discs, more on rt., 38 mononuclears, Pandy plus. Discharged 2–9–21, bright and active. 6–14–22, undernourished, chronic tonsillitis. 5–5–24, no complaints, tonsillitis, does fairly well in school. 3–15–29, no complaints, now 16 yrs. old, healthy and strong, went through 9A, no grades missed, now works in factory, reported to be the best child of a large family, sl. rt. internal squint, slight flattening of nasolabial fold, rt. Wore glasses for several years after illness but has now discarded them. Recovery.

40. 24235. C. J., aged 3 yrs. Colored male. Attack of encephalitis with hospital admission at age of 1 year 9 months (3–25–20), was drowsy, had difficulty in walking and swallowing food, mask face, painful neck, lumbar puncture showed 19 cells chiefly polymorphs, Pandy ++. T. to 104°, complete recovery. 9–20–20, short period of sleeplessness and slight overactivity. 6–10–21 deeply stuporous, questionable Kernig, 260 mononuclears, Pandy ++. Discharged 6–24–21, nearly normal. 4–1–29, no physical complaints. Neurological examination negative except for definitely more active knee-kick on left. Child reported to have failed twice in school. Binet-Simon shows scattering, but no definite mental retardation, no obvious behavior anomalies. Recovery.
41. 29809. C. L., aged 2 yrs. 5 mos. White male. Onset 8–24–21: vomiting, convulsions (generalized), coma, head retracted, T. 100.7°, 17 cells, Pandy 4 plus, congenitally cyanotic, patent interventricular septum, pulmonary stenosis. Discharged 8–31–21, improved, heart condition unchanged. 9–2–21, reported dead, details unavailable.
42. 9411. I. A., 6 yrs. Colored male. Onset 12–18–21: vomiting, headache, abdominal pain, backache, generalized convulsions, stupor, Kernig bilaterally positive, T. 101.5°, 20 cells, Pandy +, for a few days restless and destructive at night, soils bed. Discharged 1–22–22, with coarse tremor of hands when grasping, stupid expression. 8–17–25, readmitted for convulsions associated with septic sore throat; 1925, tonsillectomy; 1926, typhoid. 2–23–29, no complaints, 13 yrs. old, robust, slight speech defect which has been noted by father since tonsillectomy, pupils rather sluggish, slight intention tremor, seems bright and capable. Has missed school since because of illness but has never failed any grades. Recovery.
43. 21547. C. T., aged 8 yrs. White female. Poliomyelitis at 1 yr. with atrophy of muscles of left upper and lower leg: onset 8–19–22, frontal headache, abdominal pain, pain in back of head and neck, muscle cramps in foot, obstinate constipation, drowsiness, choked discs, T. 99.6°, 188 mononuclears, Pandy 0, colloidal gold curve 5533110000. Discharged 8–31–32, improved. 1–8–23, dizziness, drawing of face to rt., falling, urinary frequency, "no physical findings." March 1929, severe headaches for several years following illness. No petit mal attacks for several years. No difficulty in school, though she takes very little interest in it. Residuum of poliomyelitis, shown by slightly small size of left leg, sluggish KK, pes cavus, no neurological changes referable to encephalitis. Bright, alert and active. No complaints. Recovery.
44. 45713. J. T., aged 12 yrs. White male. Poliomyelitis at 16 mos. with residual paralysis of legs, and left arm. Onset 8–3–25, headache, vomiting, epigastric pain, convulsion (generalized), stupor, disorientation as to place, T. 100.4°, 25 cells, 90% mononuclears, Pandy 0. Discharged 8–14–25, well. 3–29–29, no complaints referable to encephalitis, except that his teacher and mother have noticed that at times he has been drowsy during the day.

Marked atrophy of muscles of legs and left arm which have in no way been influenced by later illness, walks with crutches. No behavior anomalies, a voracious reader and splendid student. Now 15 yrs. old, in 10B, no grades failed. Recovery.

45. 46755. W. B., aged 11 yrs. 9 mos. White male. Onset 10–13–25, headache, stupor, generalized convulsion, delirium, questionable weakness of left arm and hand, T. 104°, 60 mononuclears, Pandy +. Discharged 11–7–25 much improved. 4–8–29, letter from Boston psychiatrist to whom pt. was taken in 1928 because of scholastic difficulties: I.Q. over 130, no neurological findings, slight hyperactivity and inability to concentrate, but within limits of normal. Recovery.

46. 49719, J. N., aged 10 yrs., 5 mos. White male. Onset 6–22–26, severe frontal headache, vomiting, generalized convulsion, mild sleep inversion, overactive, irritable, profane, uncoöperative, runs around naked, bites toenails, moderately choked discs, T. 101°, 225 mononuclears, Pandy +. Discharged 7–12–26, greatly improved. 8–3–26, sleeps well, more docile. 3–9–29, no complaints, in fine physical condition, still has temper tantrums but they are much less violent than previously. Now 13 years old, in 8A, does well in school, no behavior anomalies elicited. Neurological examination neg., except for slight right internal strabismus. Recovery.

47. 58006. C. B., aged 3 yrs., 2 mos. White male. Onset 5–25–28, headache, abdominal pain, vomiting, general hyperaesthesia, stupor, delirium, stiff neck, opisthotonos, bilateral Kernig, KK not obtained, pupils dilated and sluggish in reaction to light, questionable choking of left disc, T. 39°C., 370 mononuclears, Pandy + (pharyngitis and tonsillitis also present). Discharged 7–1–28, normal except for temper tantrums which were not present before illness. 8–21–28, terrific temper tantrums. March 1929, 4 yrs. old, no complaints, temper tantrums have subsided and child is no more unstable or difficult to manage than before illness. Bright and alert, in good physical condition, KK not obtained, probably because child would not relax, questionable ankle clonus on left. Recovery.

48. 58434. T. B., aged 9 yrs. White male. Always delicate and under weight. Onset 7–1–28, headache, backache, general hyperaesthesia, vomiting, reflexes hyperactive, bilateral Kernig, sl. stupor, T. 39.8°C., 46 cells, Pandy +. Discharged 7–30–28, completely recovered. 9–4–28, no complaints, plays and sleeps well, gained 8 lbs. 4–2–29, child thin, cranky, poor appetite, has frequent headaches, attention fleeting, does poorly in school. There is nothing however which can be definitely attributed to encephalitis, since these complaints were present before the illness. Recovery.

Abortive

49. 25001. T. C., 9 yrs. White male. Onset 1–6–20, sudden overactivity, visual hallucinations, bizarre activity, poor sleep at times, spitting, throat

clearing. Admitted 5–29–20, T. 100° (reported to have risen to 104°, four months later), 38 cells, Pandy +; 6–12–20, discharged unimproved to psychiatric service because of incorrigibility. 9–15–20, reported mentally undeteriorated. 10–23–22, sits with vacant smile, strong and combative. 2–23–24, overactive, filthy, must be cared for in institution (City Hospital). July 1925, admitted to Springfield State Hospital, unable to talk or walk, extremely emaciated, trophic ulcers over back, hips and extremities, typical Parkinson; face blank, extremities spastic and tremulous, legs and left arm useless from contractures, mentally deteriorated. Died August 1925 from gangrenous ulcers.

50. 24628. W. J., aged 3 yrs. White male. Onset indefinite, at first restless at night, 1–16–20: admitted 4–23–20, sleep inversion, nocturnal hyperactivity, spitting, blowing, careless wih urine and feces, T. normal, 10 mononuclears, Pandy 0. Discharged 6–4–20, unimproved. 10–4–20, has periods without sleep lasting several days, followed by continuous sleep for as much as 30 hours. 1–12–21, no change. March 1929, questionnaire: child now in special school, delicate and "nervous," constantly in motion, voice monotonous and slow, speech defect, sometimes unable to talk, face expressionless, arms and legs weak, stiff and show jerking movements. Rectal sphincter not controlled under excitement, hands and feet always damp with sweat, drools saliva. Is now 13 yrs. old and in 4th grade in school, though mental grasp is reported better than speech would indicate. Lies, steals, cruel, tries to get own way, temper tantrums, constantly employs gesture of negation with rt. hand. Complete incapacity. Parkinson.

51. 24726. B. J., aged 6 yrs. White male. Onset 2–2–20, twitching of arms, irrational, sleep inversion, scanning speech, hyperactivity, pain and stiffness in back. Admitted 5–3–20, 2 cells, Pandy plus, T. normal. Discharged 5–31–20, sleep and speech improved. 7–15–20, better except that sleep is very bad, no sleep some nights. Died of acute abdominal condition within a year, details not obtained.

52. 23993. P. E., aged 9 yrs. White male. Onset 2–11–20. Delirium, hyperactivity, insomnia. 2–14–20, choreiform movements, rt. internal strabismus, T. 100.8°, 51 cells, Pandy +, +. Discharged 3–5–20, in good condition, but with throat-clearing tic. Readmitted 5–7–20 with typical sleep inversion and nocturnal hyperactivity, numerous tics (clearing throat, wiping nose, stretching arms and legs). Discharged 5–19–20, unimproved. 5–2–22, sleep inversion and original tics gone, more or less coincident with their disappearance beginning Parkinsonism, mentally alert: 6–17–25, unable to walk unless supported, unable to feed himself because of tremor, talks very slowly. 4–2–29, in home for incurables for last year. Completely helpless, spasticity and fine rapid tremor of extremities. Good grip in left hand, but cannot relax it. Other members useless, though occasionally with great effort short quick movements can be initiated. Face expressionless, slightly stiffer on

left, drools saliva, occasionally draws deep noisy breath. Has become obese in last few months, thus masking any muscular atrophies. Understands conversation, with great effort rips out brief answers to simple questions. Reads with enjoyment. Complete incapacity.

53. 24026. C. S., aged 7 yrs. White male. Onset 2–19–20. Nocturnal restlessness, myoclonus, delirium; 2–21–20, stupor, pain in rt. ear, arm, hand, internal strabismus, bilateral ankle clonus, T. 103°, 36 mononuclears, Pandy faintly plus; "mild attack." 3–1–20, discharged, improved. 4–26–20, typical sleep inversion with nocturnal hyperactivity, spitting; 12–20–20, sleep inversion persists, many tics, memory impaired, gait stiff, face blank. Admitted to Springfield State Hospital, 12–29–22, unreasonable, indecent, profane, screaming, cruel, stereotyped movements, loses consciousness, and is sometimes thrown down by involuntary muscular contractions, sleep inversion, unable to dress and undress, can walk but falls backward when he stops. 3–29–29, bedridden for four years, spoon-fed, typical Parkinson syndrome, tremors, spasticity, muscular atrophies and contractures of feet, face blank, drooling, coarse tremor of tongue, rapid noisy breathing on excitement, a few simple movements executed with accuracy and great rapidity after considerable effort, executes simple commands, and names common objects, speech slurring, answers after a long period of silence during which he apparently is trying to speak. Complete incapacity.

54. 24021. W. D., aged 11 yrs. White male. Onset 2–19–20, delirium, hyperactivity, T. 100.2°, no neurological changes. 2–23–20, sinks into coma, hyperpnoea, sphincter incontinence, decubitus, T. 105°, 7 cells, Pandy 0, fed by gavage. 3–12–20, left external strabismus, spasticity of extremities, bilateral Babinski and ankle clonus, coma lasts 10 weeks, during which time almost no spontaneous movements. 6–20–20, discharged improved and able to walk, gradual appearance of typical Parkinson picture quite marked by 4–15–21. 6–24–22, fights, steals, violent temper, Parkinsonism so marked that pt. frequently falls; sent to State Hospital. 9–26–23, died "from exhaustion, and decubitus, bedridden, semistuporous, occasional periods of crying, typical Parkinson with nystagmus".

55. 25225. H. B., aged 7 yrs., 10 mos. White female. Onset 2–24–20. Sleep inversion with nocturnal hyperactivity, drooling, spitting, careless with urine and feces, (spares rt. arm). Admitted 7–26–20, T. 100.8°, cells 3, Pandy 0. Discharged 8–7–20, improved. 3–18–29, mother reports sleep inversion persisted 1 yr.: that, as sleep improved pt. got gradually weaker, had difficulty in walking and five years ago became completely bedridden. Now 17 yrs. old, extremely emaciated, ht. about 4′10″, wt. about 40 lbs., underdeveloped. Rt. arm and leg weak and spastic, rt. hand and foot useless because of contractures, flexors of all extremities have some power, but extensors are too weak to overcome their pull, bilateral ankle and patellar clonus, Oppenheim pos. rt., atrophy of rt. back muscles, rt. pupil sluggish,

talks relevantly and intelligently, though with marked impairment of enunciation, but is frequently mute, and unable to swallow. Intellectual faculties impossible to test adequately, but reported as unimpaired. Mood, a combination of apathy and mild euphoria. Complete incapacity, unable to do the slightest thing for herself. Parkinson.

56. 25476. H. G., aged 9 yrs. White male. Onset 2–27–20, sleep inversion, apprehensiveness, hyperactivity; 3–1–20, left facial weakness; 7–13–20, internal strabismus. Admitted 7–12–20. Discharged 7–14–20, untreated. 12–27–20, sleep difficulty still persists. 3–25–29, questionnaire: has gotten worse since discharge, sleep poor, speech defect, overtalkative, face blank, drools saliva, partial paralysis of left arm and leg, stiffness and wasting of muscles in left arm, temper violent, memory good but does not go to school (18 yrs. old), various tics such as holding mouth open, spitting, clearing throat, clapping hands on chairs. Complete incapacity, Parkinson (atypical).
57. 30445. N. F., aged 5 years. White male. Onset 5–3–20, "eyes danced," hyperactive, sleep inversion, constant rhythmic movement of arms, many tics, hyperpnoea. Admitted 11–3–21. Discharged 11–7–21, sleep good but otherwise unimproved. 4–3–29, questionnaire: often drowsy and indifferent, speech monotonous and slow, speech defect, face blank, drools saliva, urinary incontinence, rapid noisy breathing, weakness and tremor of arms and legs, unable to look after his own wants, memory poor, 14 yrs. of age and in the 3rd grade. Ht. 4′ 8″, wt. 110 lbs. Pt. becomes blue when he stops puffing. Constant movement of hands. Complete incapacity. (Parkinson.)
58. 25380. M. B., aged 5 yrs., 5 mos. White female. Onset May 1920, with sudden excitability, spitting and sleep inversion. Alternates between periods of stupor lasting a few days and wild nocturnal activity. Voided and defecated in bed. Admitted 7–6–20. Discharged 7–11–20, with sleep slightly improved. Reverted in a week and admitted to another hospital whence after 2 mos. she was discharged as improved. 4–3–29, mother reports that sleep inversion persisted for about three years from onset. Has drooled, been violent, noisy and almost unmanageable until last two years. Is still self-willed and forward, and is managed with difficulty. Still puffs, blows and spits a great deal. In spring of 1928 for 5 wks. her face was blank, drooling, spasticity of right arm and leg, irregular twitching of limbs and body. Present examination negative except for slight internal strabismus, slight suppression of reflexes of rt. arm and rt. leg, irregular twitching of trunk and limbs which is much worse after fatigue. Started school at 9, very irregular in attendance, now goes only in afternoon, in 3rd grade, forgetful and very difficult to teach, reads much with evident enjoyment. Partial incapacity. Parkinsonian features.
59. 21410. J. M., aged 8 yrs. White male. Onset 2–7–21, hyperactivity, insomnia, visual hallucinations, disorientation, T. 103°, 70 cells, Pandy plus, Bright in morning, sleepy in afternoon and night. Discharged 3–6–21,

normal except for tendency to sleep during day. 4–2–21, emotionally unstable, recent memory poor, typical sleep inversion, tics of mouth and eye. 10–18–22, sleep improved, hard to rouse in morning, still slightly hyperactive, memory is improved. 9–22–21, spitting, hyperactivity, sleep inversion, memory bad but gets along in school. Sept. 1928, seen in psychiatric clinic. Now 16 yrs. old, a disciplinary problem, expelled from first year of high school for insubordination, threatens and terrifies mother, masturbates openly. Neurological examination shows only coarse tremors of hands and tongue. Binet-Simon test scatters, average adult intelligence. April 1929, reported to be holding a job with fair success. Partial incapacity.

60. 34839. W. R., aged 3 yrs. 7 mos. White male. Onset 1–17–23, sleep inversion, incontinence, decorates feces, overactivity, overtalkativeness, "tabetic facies" without facial nerve paralysis, ataxia of extremities, slight difficulty in pronouncing words, T. 101°, 4 cells, Pandy 0. Discharged 2–26–23, quieter, able to sleep after midnight. 3–15–29, mother reports that sleep inversion persisted 14 months from time of discharge, spitting, drooling not so persistent, very fearful for two years, face expressionless for a long time. At present only residuum of illness is rapid noisy breathing on excitement. Now 9 yrs. old, started school at 6, in 3 A, has skipped one grade and does very well. High-spirited, occasionally very mean when crossed, petty lying and stealing, often kept in at school (an only child and spoiled). Neurological examination negative, recovery. Transient Parkinsonian features.

61. 54240. J. F., aged 9 yrs. Onset January 1925, fever, diplopia, "nervousness," twitching of the extremities, mild sleep inversion. Seen in dispensary 7–2–25, suggestion of mask face, frequent stretching and arching of back, impression—beginning Parkinsonism. 6–18–27, sent to special school because of incorrigibility, sleep improved, spells of deep breathing followed by periods of apnoea, frequently blows through fingers and over back of hand, behavior best described as "fresh," 8% albumin in urine on one occasion. 10–20–27, physical condition excellent, behavior better. 4–6–29, still at special school but showing marked improvement, blows only when excited or alone, occasionally tears clothes apparently to hear the sound, still overtalkative and somewhat fresh but easily controlled, no temper outbursts. Physical condition good. Binet-Simon test—scatters through fourteen years, chronological age 13 yrs. 2 mos., mental age 12 yrs. 4 mos. Doing 6th grade work with a private tutor. Partial incapacity.

Meningeal and somatic

62. 24903. M. J., aged 8 yrs. White male. Onset 5–18–20, inability to talk, transient right hemiplegia, right facial weakness, spares left arm though nothing definite made out, neck stiff. Kernig positive. 250 cells 80% PMN, Pandy plus; later (6 days) 66 cells mononuclears, Pandy plus, T. 100.2°, very drowsy. Discharged 6–6–20, completely well. 3–22–29, health better

since illness. Now 17 years old, stopped school one year ago in 9A, no scholastic difficulties, no trouble holding job, neurological neg. Complete recovery.

63. 45862. J. H., aged 5 yrs. 5 mos. White male. Onset 8–14–25, convulsions with twitching of left side, stupor, irrationality, irritability, rt. facial weakness, unable to stand, low grade choked discs with exudate in lower rt. fundus, head slightly retracted, Kernig and Brudzinski suggestive, T. 102.4°, 216 cells, Pandy plus, colloidal curve 23321000000. Discharged 9–12–25, greatly improved. 11–18–25, rt. facial weakness still present, urinary incontinence day and night since illness. 4–3–29, incontinence still continues, always moving, easily excited, cries a lot, afraid of dark, bites nails, constant coughing and clearing throat (drooled for a month following illness). Now 9 yrs. old, started school at 7, in 1A, does very poorly. Older brother (2 yrs.) who also started at 7 was in 2A at 9, does not exhibit the neurotic traits of the pt. Neurological exam. neg. Speech indistinct but has been so since birth. Partial incapacity.

Unclassified because of insufficient history

64. 52825. E. V., aged 2 mos. White female. Onset 1920, when she looked "as though she had been doped." Not seen until 4–8–27 at age of 7 years, right pupil fixed, sluggish, larger than left, facial weakness, left half of tongue atrophied, left hand continually clenched, varus deformity of feet more marked on left, drooling, constant movements of arms and head, blank expression, mentally retarded. April 1929, questionnaire: no essential change in picture, left arm and leg described as atrophied and paralysed, speech monotonous and slow, slurring, child only partially able to look after her own needs, runs away, difficult to manage, mentally slow, does not go to school. Parkinson (?) Complete incapacity.
65. 57550. E. J., aged 7 yrs. White female. Onset indefinite in 1925, no history of febrile illness. Slight spasticity of left face, marked tremor and spasticity of left arm, slight spasticity of left leg, loss of associated movements of left arm when walking, when excited has choreo-athetoid movements of trunk, neck, and rt. arm, 1 cell, Pandy 0. Admitted 4–26–28 for diagnosis. Discharged following day. April 1929, questionnaire: picture essentially unchanged during past year except in degree, child has gotten worse, weakness, tremor, spasticity, and muscular atrophy of left arm, slight tremor, spasticity, and atrophy of left leg, slight spasticity of left face. No important behavior difficulties, does well in school. Unilateral Parkinsonism (?) Partial incapacity.
66. 49767. R. S., aged 6 yrs. White male. Onset Feb. 1926, a febrile illness of one week's duration. T. 103–104° followed by a period during which the child threatened to be a chronic invalid. Irritability, pugnacity, violent temper tantrums were sequelae of this illness and were felt by the Phipps Psychiatric

clinic (6–30–26) to be on an organic basis. A peculiar tic of rolling the eyeballs downward with lids wide open was also noted. 3–10–29, questionnaire: child is more delicate than others. Complains of aching in legs, behavior anomaly disappeared two years after illness, now has pleasant disposition, easily controlled. Now 9 years old, in 3rd grade, does excellently in school. Complete recovery as regards behavior anomaly.

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OBSERVATIONS ON THE PLACENTA FROM A CASE OF MALARIA[1]

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The diagnostic value of the placental blood film in aestivo-autumnal malaria has been pointed out by Clark[2] ('15). He concludes that this type of malaria, when associated with labor and the early days of the puerperium, can be more easily and certainly diagnosed by the use of this film and a polychrome stain than by employing the usual films made from the mother's peripheral blood at the time of labor. Moreover, by this method the early days of the puerperium many times can be protected from a malarial outburst, and, as a rule, puerperal sepsis can be differentiated.

Clark adds that malaria frequently interrupts the late stages of pregnancy and sometimes causes the death of the mother and the fetus, more often the latter. The commonest mishap is miscarriage late in pregnancy. Occasional still-births occur and sometimes there is a fatal issue to both the mother and child.

Transmission of malaria from mother to fetus is a rare circumstance. Clark states that cases diagnosed as congenital malaria probably indicate that some accident had occurred to the placenta, because fetal blood is practically never positive at the time of birth, regardless of the degree of infection in the mother. He believes that many of the cases now reported as congenital malaria suggest immediate postnatal infection as their history, as the pathological and clinical records testify.

Finally, in reference to the rôle of the placenta in malaria, Clark says that a sluggish blood-sinus with a large endothelial surface, a higher internal body temperature, and red blood-cells burdened with parasites of a certain age beyond the ring form, seem to be important factors in the localization and development of the aestivo-autumnal

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[2] Clark, H. C. 1915. The diagnostic value of the placental blood film in aestivo-autumnal malaria. *Exp. Med.*, vol. 22, p. 427.

parasite. It appears that the intricate vascular architecture of the mature placenta rivals that of the spleen, liver and bone-marrow as a harbor for adult malarial parasites of this type and as a storage for pigment. And furthermore, according to Clark, the size of the intervillous spaces of the placenta and their adaptability in the localization of parasites seem to disprove to a certain extent the old idea that the localization depends on the smallness of the capillary caliber. If this were the case, the brain should be more often the seat of an extensive localization than the spleen, bone-marrow, and placenta, yet the anatomical records will not support that theory.

In spite of the fact that Clark points out the importance of the placenta as a site of localization of malarial parasites, and emphasizes the usefulness of the examination of placental blood films, no one appears to have subjected this organ to microscopic examination in cases of malaria.

The present observations were made on the placenta from a case of malaria and are deemed sufficiently important to be reported. The material was presented to me by Dr. Clark. It consists of a number of blocks of placental tissue fixed in Zenker's fluid or in 10-percent formalin.

The tissue is from a woman suffering from malaria who was admitted to the Santo Tomas Hospital, Panama (case no. 93632). The woman received five hypodermic injections of quinine (7½ grains each) in the two and one half days prior to her delivery. Her peripheral blood film (thin film examination) was negative on the day of delivery. At the time of admission her temperature was 102°F. She was delivered of a child weighing 6 pounds 8 ounces.

The blocks of tissue were imbedded in celloidin and sectioned. The sections were stained in haematoxylin and eosin and in Mallory's connective-tissue stain.

Accompanying the blocks of tissue is a film of placental blood obtained by scraping the maternal surface of the fresh placenta and preparing a film as for blood cells. This preparation is stained with Wright's stain. Examination of this slide reveals an interesting picture. There are in the film a great number of erythrocytes many of which contain segmenting and presegmenting forms of the malarial organism identical in configuration with the forms pictured by Clark

('15) in similar preparations. It is of interest that, in spite of the quinine treatment and the absence of parasites in the peripheral blood, the placental blood film should show such a high frequency of parasites.

The other categories of cells in the placental film are equally of interest. The majority of the cells of which there is a great abundance are mononuclear. These can be divided roughly into two groups, one composed of lymphocytes, the other of typical monocytes. Besides the usual but sometimes rather unsatisfactory morphological criteria for separating these two cell strains in Wright's stained preparations there is in the present instance a criterion for the recognition of the monocyte. This consists in the exhibition, by a fraction of the mononuclear cells in question, of malarial pigment (melanin) in their cytoplasm. To all intents and purposes the phagocytosis and storage of the pigment amount to a vital staining of the monocytic cells which stand out in bold relief due to this phenomenon. The cells so documented constitute approximately one-quarter of the total number of the nucleated cells under consideration. The pigment has been stored in the cytoplasm of the cells in the characteristic manner in which a supravital dye, neutral red for example, is distributed. The nuclei of these cells are eccentrically placed and are for the most part indented. In the cytoplasm contiguous to the indentation of the nucleus, the pigment has become concentrated, varying in amount from a few granules up to a large cluster of granules including aggregates of pigment of considerable size. The configuration of the cluster is in every way analogous to the rosette formation seen in neutral red preparations. There is a uniformity about the pattern which is striking. Cells, tremendously laden with pigment, with an irregular disposition of the masses which partly obscure the nucleus, as seen in the pulmonary alveoli, or in the peritoneal cavity after the experimental introduction of finely dispersed carbon, are not encountered. In other words, none of the cells observed approach, in the degree of phagocytosis, the cells typically designated as clasmatocytes.

Clark ('15) in his paper on placental blood films in malaria speaks of the phagocytosis of pigment by mononuclear cells, but he refers to them as lymphocytes, whereas the present investigator from the observations given prefers to classify the phagocytic cells as monocytes.

The lymphocytes in the present preparation differ morphologically from the monocytes and in addition do not phagocytize the malarial pigment.

Besides these two strains of cells, lymphocytes and monocytes, the preparation contains a few polymorphonuclear leucocytes which in the present instance are not phagocytic. A few large cells, epithelial in character, undoubtedly of local placental origin, are present.

The only other cells found in some number in the preparation are nucleated erythrocytes: normoblasts in considerable abundance (4 per cent) and late erythroblasts only in small numbers. That these cells, for the most part, are not fetal in origin, and that they have not escaped from torn chorionic blood-vessels, seems likely for several reasons: very few nucleated red cells are ordinarily encountered in the fetal circulation during the last months of pregnancy, and secondly, on examining sections of the placenta, nucleated red blood corpuscles are found in the intervillous spaces. The presence of nucleated erythrocytes in the intervillous spaces must be attributed to a secondary anaemia in the mother.

Examination of the sections of the placenta reveals the chorionic villi and the intervillous spaces. The latter contain a greater amount of blood than usual and a large quantity of non-granular leucocytes, which are distinguishable here, as in the blood film, as lymphocytes, on the one hand, and as pigment-laden monocytes on the other. Nucleated erythrocytes are also present in the intervillous space.

On the part of the fetal tissues there is no visible reaction to the presence of the parasites or their products. The chorionic villi appear normal. There is no reaction on the part of the fetal stroma, nor is the chorionic syncytium which clothes the villi and lines the intervillous space, retaining the maternal circulation within its confines, in the least abnormal. This observation is of some interest from the standpoint of the function of the chorion. We are dealing in the present instance with a phenomenon analogous to vital staining in that, in malaria, there is present in the maternal circulation a quantity of pigment, in part at least as melanin, released from the malarial parasites. The melanin may be regarded as a fine particulate suspension which is subject to phagocytosis and passage through endothelial and serous surfaces. In the present specimen, however, no trace of

pigment is found in the chorionic syncytium nor in the underlying fetal stroma. The syncytium is neither permeable to, nor phagocytic for, such finely divided matter. This surface possesses a different order of permeability and has a higher threshold for the passage of inert substances than membranes composed of either endothelial cells or mesothelial cells. This belief is of course current from experimental observations on placental transmission in animals, as well as from chemical analyses of maternal and fetal blood samples in man and in animals, but the present observations bring rather direct proof in man of the validity of the statement.

From the lack of any abnormality of the intact syncytial surface it appears even less likely that the chorionic ectoderm transmits the malarial parasites themselves from mother to fetus.

Examination of the sectioned material brings up another observation for discussion. As is well known, fibrin is deposited in various parts of the placental labyrinth during the latter half of pregnancy. These masses of fibrin are attached to the villi which become denuded of syncytium to some extent where the fibrin has formed. This may be regarded as a degenerative or senescent phenomenon which gradually overtakes the placenta, possibly representing in some measure a factor contributing to the termination of pregnancy.

Whether these fibrinous areas have a greater or lesser degree of permeability than the portions of the villi clothed by syncytium is unknown. These fibrinous areas are sparsely infiltrated by cells, the character and origin of which in ordinary sections of placenta it is difficult to ascertain. In the present malarial placenta, however, the deposits of fibrin attached to the locally denuded villi are found infiltrated by the pigment-bearing monocytes. The monocytes come in places in contact with the fetal stroma without seeming to enter it. This observation raises the question of the differential permeability of the villi where they are covered by intact syncytium and where they are covered by fibrin. It is possible that the fibrinous areas represent to some extent a partial breaking-down of the placental barrier, which may have a bearing on the time at which immunity towards certain substances becomes established in the fetus.

The further question arises as to what extent the blood picture described in the intervillous spaces and in the placental blood film

differs from the normal blood picture of this locality. To answer this question a number of supposedly normal placentae have been subjected to examination. Placental blood films from these favorable instances have been counted differentially.

As a result of these examinations, it appears that in malaria the total or absolute number of white cells in the intervillous spaces is vastly increased. Normal placental blood, on the contrary, contains white cells in ratios very nearly equivalent to peripheral counts, excepting for a slight shift towards an increased percentage of lymphocytes. In the malarial placenta, on the other hand, there is an absolute and relative increase in both lymphocytes and monocytes, reducing the number of polymorphonuclear cells seen to about six per cent. The sluggish circulation of the placental labyrinth appears to favor under normal circumstances the accumulation or retention of a certain number of lymphocytes. In malaria, however, several additional factors—the presence of an increased number of lymphocytes and monocytes in the circulating blood, as well as the liberation of relatively large amounts of pigment from the malarial parasites localized in the placenta—make the accumulation of cells in the placental labyrinth readily understandable. Although the placenta has, like the spleen, bone-marrow and liver, a labyrinthine, sinusoidal circulation, supposedly favoring retention of certain kinds of cells, it is unlike those organs in that blood cells are not produced from the walls of its intervillous spaces. The cells encountered in the intervillous spaces must have been brought there from distant organs via the circulation.

The malarial parasites are relatively immune to damage in the placental circulation as witnessed by their abundance in the placental blood film after quinine treatment had eradicated them from the peripheral circulation. In spite of their great numbers in the intervillous spaces they produce no visible pathological changes in the chorionic syncytium or in the underlying stroma of the villi. The syncytial membrane intermediating the nutritive transfer from mother to fetus appears to be anatomically normal. Nevertheless, it is known that malaria frequently interrupts the late stages of pregnancy, as well as occasionally causing death of the fetus. These results cannot, however, be correlated with direct, visible alteration of the placental tissue, but must be due, in case of death of the fetus, to invisible,

noxious substances acting upon fetal tissues which are, as far as we can ascertain, grossly and microscopically normal.

SUMMARY

1. The study of the placenta from a case of malaria affords proof that the chorionic syncytium is incapable of phagocytizing an inert suspension of pigment present in the intervillous spaces or of transmitting such particles from mother to fetus.

2. Malarial parasites are present in the placenta in great abundance within the erythrocytes in the intervillous spaces.

3. Malaria induces the accumulation of large numbers of monocytes and lymphocytes in the placental circulation. Of these cells, the monocytes phagocytize, abundantly, pigment released by the activity of the malarial organisms. These phagocytic monocytes do not penetrate the fetal tissues, but do enter the masses of fibrin formed on the villi which are denuded of syncytium at these sites. Typical clasmatocytes are not encountered in the intervillous spaces. The monocytes and lymphocytes which gather in the placenta are brought there from other parts of the maternal body where they are produced.

4. The villi, including their stroma and covering chorionic syncytium, are anatomically normal and not visibly affected by the malarial organisms or their products. It is unlikely that malarial organisms can enter or penetrate the chorionic syncytium, so that the transmission of malaria from mother to fetus occurs rarely, if at all.

THE VIEWS OF ADAM SMITH ON MEDICAL EDUCATION

MANFRED S. GUTTMACHER

Eighteenth Century England produced no greater academic figure than Adam Smith. He was unquestionably the foremost political economist of the world. Only Edmund Burke and Turgot were to be compared with him. But they were great political leaders, interested in practical statesmanship rather than in economics and political science. Adam Smith was preeminently a scientist. He had that remarkable breadth of scientific interests that stamped the great leaders of his century. He occupied university chairs in Rhetoric and Belles-Lettres, in Logic, and in Moral Philosophy, and finally he became Lord Rector of the University of Glasgow.

His long period of association with the two great universities of Scotland, his six years' fellowship at Oxford and his three years in Europe as travelling tutor to the third Duke of Buccleugh, mark him as one preeminently fitted to discuss the educational theories of his day.

During the ten years from 1745 to 1755 when William Cullen worked so hard to establish an efficient medical school at the University of Glasgow, Adam Smith was one of the most important members of the faculty of that university. Unquestionably, he took a keen part in Cullen's efforts. Few persons knew that while preparing his great work, "The Wealth of Nations," for publication, Smith, with Gibbon, the historian, attended the anatomical lectures of William Hunter at the Great Windmill Street School. Smith was then past forty years of age.

In 1774 he wrote at the request of Cullen, then the great leader of the medical school of the University of Edinburgh, a very remarkable letter, giving in detail his views on medical education. His letter was first published, in 1832, by Thomson in his biography of William Cullen. The letter was republished in 1895 in John Rae's splendid biography of Smith. I feel that it has received too little attention from medical educators and is deserving of resurrection for publication

in a medical journal. Many of its basic thoughts are as pertinent for our day as they were then, more than 150 years ago. Written in Smith's lucid style, much of its content is plain enough. Yet the general situation then existent in regard to the conferring of university degrees and certain specific allusions require some explanation. Rather than interrupt the letter's context, I should like to offer certain anticipatory notes.

Since 1771, the Scotch University Degree Scandal had been much in prominence both in England and Scotland. The two smaller Scotch Universities, St. Andrews and Aberdeen, because of straitened finances, were selling degrees promiscuously to non-resident applicants. To obtain a medical degree, it was necessary to forward ten guineas (at the end of the century, according to Fessenden, £12, 2 s., 6 d. were required) and the endorsement of two licensed practioners. These endorsements, often spurious, were, moreover, never investigated.

This practice had been going on for many years. In 1754, William Hunter wrote concerning it to William Cullen, his first medical teacher, whom he once described as the "man to whom I owe most and love most of all men in the world":

> "You no doubt know how contemptuously the College of Physicians here have treated all Scotch degrees indiscriminately. . . . . You can hardly be ignorant that the professors, of one Scotch University at least, shamefully prostitute their degrees still to anyone who can pay them a small sum of money and procure, perhaps purchase, a recommendation from some necessitous doctor. There is something so mean, and so unbecoming gentlemen in this, that I dare not say anything further upon it, for fear of writing with unbecoming warmth. . . . . We therefore wish that you would be so kind as to coöperate with us to bring about, if possible, some general resolution of the Universities in Scotland with regard to degrees."

In 1771 Samuel Leeds, a Doctor in Physic of the University of Edinburgh, proved so incompetent in his duties at the London Hospital that its board of governors made the continuance of his tenure of office dependent upon his passing the examinations of the London College of Physicians. He failed this examination ignominiously.

After his arrival in London from Scotland, he had been espoused by several leading persons among the Quakers. Shortly after his successful election as physician to the London Hospital, one of his colleagues, in a conversation with Dr. John Fothergill, the great Quaker doctor,

happening to mention Leeds' success, was warned, "Take care he do no mischief."

Leeds learned of this, and after his dismissal from the hospital sued Dr. Fothergill. A board of arbitrators, by a vote of three to two, awarded him £500 damages. Fothergill sent his brother to Edinburgh to investigate Leeds' record at the University. Legal proof was adduced that the exercises were not performed by himself which he had produced as his own. It was further proved that he knew not one word of Latin or Greek. Cullen was at this time the only man lecturing in English, and all papers and theses were required to be written by the students in Latin. Dr. Fothergill brought the case before Lord Mansfield, one of the two greatest jurists of the century. He refused to hear Dr. Fothergill's counsel, because, he observed, the evidence on the part of Dr. Leeds' arbitrators was sufficient to prove the illegality and injustice of their own award. He further added that Dr Fothergill did no more than his duty in saying what he was charged with; and that he would not have acted as an honest man had he said less.

Within the medical profession there was for some time a very bitter feeling toward Fothergill for having had recourse to the courts in a matter which was believed to have belonged within the Aesculapian Guild; so that when, shortly after this, the by-laws of the London College of Physicians had been changed to admit physicians who were not graduates of Oxford and Cambridge and Dr. Fothergill was proposed, he was defeated by a vote of 13 to 9. The Leeds' incident brought to the fore conditions in the Scotch Universities. For some years it formed a constant topic for disputation in the medical circles of England and Scotland.

Jean Paul Marat, the great leader of the French Revolution, who for some time practiced medicine in Soho, bought a medical degree from St. Andrew's University in 1775. It was at about this time that two of England's most successful itinerant quacks, William Brodum and Samuel Solomon, bought their diplomas from Mareschal College and the University of Aberdeen. These very clever German Jews advertised themselves as F. R. H. S.—Fellows of the Royal Hibernian Society—a non-existent body. In a fifty-fourth edition of Solomon's "Guide to Health or Advice to Both Sexes," which I possess, he prints

an English translation of his diploma. John Kay, that remarkable barber cartoonist, published a delightful engraving, "The Sapient Septem Viri," representing the professors of the various faculties of Mareschal College of Aberdeen hawking diplomas. The professor of Physic cries, "Degrees Male and Female in Medicine and Midwifery sold for ready money."

In 1774, the third Duke of Buccleugh was elected as Honorary Fellow of the College of Physicians of Edinburgh, of which William Cullen was then the president and guiding spirit. The Duke offered to take up in the Scottish Parliament the question of the requirements for medical degrees. The College formulated the following Memorial for him to present:

"MEMORIAL"

"The Universities of St. Andrew's and Aberdeen have frequently given degrees in absence; that is, have conferred degrees by diploma on persons who never appeared before them to undergo any examination; and they confer the degree merely upon a certificate of two physicians, declaring that they judge the candidate or person recommended to be worthy of a degree in physics. Very often the physicians thus certifying are obscure persons, and as little known to the University as the person they recommend; and sometimes it may be presumed that the certifying physicians are very little qualified to judge of medical knowledge and abilities. In short, it is alleged, and commonly believed, that little else than the payment of the usual fees is necessary to obtain such a degree.

"Farther, the same Universities of St. Andrew's and Aberdeen, when conferring degrees upon persons present and undergoing examination, do, however, admit persons to such examination without any evidence of the candidate's having applied regularly to the study of physics, or of his having made any residence for that purpose in any University where the several branches of medical study are properly taught. How the examinations, in such cases, are conducted, it is not possible to say, in general; but, from some instances of persons who have received such degrees, it is strongly suspected that the examinations are not strict or rigorous.

"It is to be observed, that the University of Glasgow, though they do not commonly give degrees in absence, yet they often give degrees, without requiring any certificate of the candidate's previous study.

"These practices are considered as an abuse. A degree in physic is, or should be, considered as the testimony of proper judges, in favour of the medical knowledge and abilities of the person who holds the degree, and, at least, it should be considered as a certificate of a person's having regularly, and for a due length of time, applied to the study of physic; but, as a degree, conferred as above, cannot be viewed in any of these lights, the practice of conferring such degrees must be

considered as an abuse of the institution, an imposition upon the public, and a matter of constant reproach speciously thrown upon all Scotch degrees.

"The abuses complained of are particularly a hardship upon the Royal College of Physicians of Edinburgh, who are obliged by their charter to grant licences, without examination, to any person who has obtained a degree from any of the Universities of Scotland.

"It is presumed, that every man who has a regard to the public good, and to the honour of Scotch literature, will be zealous to have the above mentioned abuses corrected, and the practice reformed; but the means of obtaining this appears to be somewhat difficult.

"There is no certain and effectual means of correcting the irregular practices of the Universities of Scotland, but by a Royal Visitation; that is, by his Majesty's granting a Commission to certain persons to inquire and to correct, as they shall see cause.

"Such a Commission, however, is to be passed under the Great Seal, and is to be directed to some persons of high rank and distinction, who must necessarily repair to the several Universities, and in this and other respects take a great deal of trouble. It is doubted if his Majesty's ministers will readily engage in such expense and trouble; and we would therefore wish to find some other method that might be more easily and readily executed.

"But if it shall be found improper to have his Majesty's power exercised, or name employed, in any other way than by a Commission, it is supposed, that any person in high office, and particularly the Secretary of State for the Northern Department, might, even in a private capacity, give an advice or admonition, to the administrators of the Universities, to have certain notorious abuses corrected.

"It is presumed that such an admonition would be attended to, as it might be understood as a threatening that, if the admonition was neglected, it might be followed by a Visitation, which, we know well, has the power of distressing disobedient members; and, as the benefit arising from the conferring of degrees in the manner above mentioned is only considerable with respect to a single member of the University, that is, the Professor of Physic, and very small with respect to the whole community, it is therefore supposed that a slight injunction will be sufficient to engage most of the members of the University to join in correcting an abuse which truly dishonours the Society.

"If it shall be thought proper to give any injunction to the Universities, it is humbly suggested that it should be simple, and with respect to the two following particulars only.

"First, That they be enjoined to give no degrees in absence, but such as are honorary and given without fees, to persons of rank and distinction, or to persons who had given some public specimen of their literature and medical knowledge.

"Secondly, That, in giving degrees to persons present, and willing to undergo a proper examination, they shall not admit any person as a candidate, who does not bring a proper certificate of his having resided for two years at least in a University

wherein physic is regularly taught, and of his having applied to all the branches of medical study.

"It may be justly doubted if the two years' residence here proposed is enough for acquiring a tolerable knowledge in physic; but it is taken from a late regulation of the Royal College of Physicians at London, who have made it a condition with respect to the licentiates they are to admit.

"It is not doubted that, in every University, the University Senate has full power to make the regulations proposed, and has also an opportunity of securing the observation of them, as no degree is at any time conferred without the consent of the Senate, or diploma granted that is not subscribed by a majority of the members.

"In directing any injunction to the Universities, it may be considered how far it is proper and necessary to address it to the several Chancellors, from whose authority every academical degree is supposed to proceed; or if it may be addressed to the more immediate administrators of the University; that is, to the Rector, Principal, and other members of the University Senate, without whose concurrence it is believed that no new regulations in the University can be made."

Before presenting it, the Duke and Dr. Cullen decided to submit it to Adam Smith for his opinion. Smith had been an associate of Cullen on the faculty of the University of Glasgow, and was greatly admired by him. From 1759 to 1762, he had been the travelling European tutor of the Duke of Buccleugh and had retained his pupil's admiration. It seems only natural that they should have turned to him, for personal reasons and because he was probably better equipped to give advice about policies of university education than any man of his day. Adam Smith's reply follows:

"My dear Doctor—I have been very much in the wrong both to you and to the Duke of Buccleugh, to whom I certainly promised to write you in a post or two, for having delayed so long to fulfil my promise. The truth is that some occurrences which interested me a great deal, and which happened here immediately after the Duke's departure, made me forget altogether a business which, I do acknowledge, interested me very little.

"In the present state of the Scotch Universities, I do most sincerely look upon them as, in spite of all their faults, without exception the best seminaries of learning that are to be found anywhere in Europe. They are perhaps, upon the whole, as unexceptionable as any public institutions of that kind, which all contain in their very nature the seeds and causes of negligency and corruption, have ever been or are ever likely to be. That, however, they are still capable of amendment, and even of considerable amendment, I know very well, and a Visitation[1] is, I believe,

[1] That is, a Royal Commission.

the only proper means of procuring them this amendment. Before any wise man, however, would apply for the appointment of so arbitrary a tribunal in order to improve what is already, upon the whole, very well, he ought certainly to know with some degree of certainty, first, who are likely to be appointed visitors, and secondly, what plan of reformation those visitors are likely to follow; but, in the present multiplicity of pretenders to some share in the prudential management of Scotch affairs, these are two points which, I apprehend, neither you nor I, nor the Solicitor-General nor the Duke of Buccleugh, can possibly know anything about. In the present state of our affairs, therefore, to apply for a Visitation in order to remedy an abuse which is not perhaps of great consequence to the public, would appear to me to be extremely unwise. Hereafter, perhaps, an opportunity may present itself for making such an application with more safety.

"With regard to any admonition, or threatening, or any other method of interfering in the affairs of a body-corporate which is not perfectly and strictly regular and legal, these are expedients which I am convinced neither his Majesty nor any of his present Ministers would choose to employ either now or at any time hereafter, in order to obtain an object even of much greater consequence than this reformation of Scotch degrees.

"You propose, I observe, that no person should be admitted to examination for his degree, unless he brought a certificate of his having studied at least two years in some University. Would not such a regulation be oppressive upon all private teachers, such as the Hunters, Hewson, Fordyce, etc.? The scholars of such teachers surely merit whatever honour or advantage a degree can confer much more than the greater part of those who have spent many years in some Universities, where the different branches of medical knowledge are either not taught at all, or are taught so superficially that they had as well not be taught at all. When a man has learned his lesson very well, it surely can be of little importance where or from whom he has learnt it.

"The monopoly of medical education which this regulation would establish in favour of Universities would, I apprehend, be hurtful to the lasting prosperity of such bodies corporate. Monopolists very seldom make good work, and a lecture which a certain number of students must attend, whether they profit by it or no, is certainly not very likely to be a good one. I have thought a great deal upon this subject, and have inquired very carefully into the constitution and history of several of the principal Universities of Europe; I have satisfied myself that the present state of degradation and contempt into which the greater part of these societies have fallen in almost every part of Europe arises principally, first, from the large salaries which in some Universities are given to professors, and which render them altogether independent of their diligence and success in their professions; and secondly, from the great number of students who, in order to get degrees or to be admitted to exercise certain professions, or who, for the sake of bursaries, exhibitions, scholarships, fellowships, etc., are obliged to resort to certain societies of this kind, whether the instructions which they are likely to receive there are or

are not worth the receiving. All these different cases of negligence and corruption, no doubt, take place in some degree in all our Scotch Universities. In the best of them, however, these causes take place in a much less degree than in the greater part of other considerable societies of the same kind; and I look upon this circumstance as the real cause of their present excellence. In the medical College of Edinburgh in particular the salaries of the Professors are insignificant. There are few or no bursaries or exhibitions, and their monopoly of degrees is broken in upon by all other Universities, foreign and domestic. I require no other explication of its present acknowledged superiority over every other society of the same kind in Europe.

"To sign a certificate in favor of any man whom we know little or nothing about, is most certainly a practice which cannot be strictly vindicated. It is a practice, however, which from mere good-nature and without interest of any kind the most scrupulous men in the world are sometimes guilty of. I certainly do not mean to defend it. Bating the unhandsomeness of the practice, however, I would ask in what manner does the public suffer by it? The title of Doctor, such as it is, you will say, gives some credit and authority to the man upon whom it is bestowed; it extends his practice and consequently his field for doing mischief; it is not improbable, too, that it may increase his presumption and consequently his disposition to do mischief. That a degree injudiciously conferred may sometimes have some little effect of this kind, it would surely be absurd to deny, but that this effect should be very considerable I cannot bring myself to believe. That Doctors are sometimes fools as well as other people, is not, in the present times, one of those profound secrets which is known only to the learned. The title is not so very imposing, and it very seldom happens that a man trusts his health to another merely because that other is a doctor. The person so trusted has almost always either some knowledge or some craft which would procure him nearly the same trust, though he was not decorated with any such title. In fact, the persons who apply for degrees in the irregular manner complained of, are, the greater part of them, surgeons or apothecaries, who are in the custom of advising and prescribing, that is, of practising as physicians; but who, being only surgeons and apothecaries, are not fee-ed as physicians. It is not so much to extend their practice as to increase their fees, that they are desirous of being made Doctors. Degrees conferred even undeservedly upon such persons can surely do very little harm to the public. When the University of St. Andrew's very rashly and imprudently conferred a degree upon one Green, who happened to be a stage-doctor, they no doubt brought much ridicule and discredit upon themselves, but in what respect did they hurt the public? Green still continued to be what he was before, a stage-doctor, and probably never poisoned a single man more than he would have done though the honors of graduation had never been conferred upon him Stage-doctors, I much observe, do not much excite the indignation of the faculty; more reputable quacks do. The former are too contemptible to be considered as rivals. They only poison the poor people; and the copper pence which are thrown up to them in

handkerchiefs could never find their way to the pocket of a regular physician. It is otherwise with the latter: They sometimes intercept a part of what perhaps would have been better bestowed in another place. Do not all the old women in the country practise physic without exciting murmur or complaint? And if here and there a graduated Doctor should be as ignorant as an old woman, where can be the great harm? The beardless old woman, indeed takes no fees; the bearded one does, and it is this circumstance, I strongly suspect, which exasperates his brethren so much against him.

"There never was, and I will venture to say there never will be, a University from which a degree could give any tolerable security that the person upon whom it had been conferred was fit to practise physic. The strictest Universities confer degrees only upon students of a certain standing. Their real motive for requiring this standing is that the student may spend more money among them and that they may make more profit by him. When he has attained this standing, therefore, though he still undergoes what they call an examination, it scarce ever happens that he is refused his degree. Your examination at Edinburgh, I have all reason to believe, is as serious, and perhaps more so, than that of any other University in Europe; but when a student has resided a few years among you, has behaved dutifully to all his Professors, and has attended regularly all their lectures, when he comes to his examination I suspect you are disposed to be as good-natured as other people. Several of your graduates, upon applying for license from the College of Physicians here, have had it recommended to them to continue their studies. From a particular knowledge of some of the cases I am satisfied that the decision of the College in refusing them their license was perfectly just; that is, was perfectly agreeable to the principles which ought to regulate all such decisions; and that the candidates were really very ignorant of their profession.

"A degree can pretend to give security for nothing but the science of the graduate; and even for that it can give but a very slender security. For his good sense and discretion, qualities not discoverable by an academical examination, it can give no security at all; but without these, the presumption which commonly attends science, must render it in the practice of physic ten times more dangerous than the grossest ignorance, when accompanied, as it sometimes is, with some degree of modestly and diffidence.

"If a degree, in short, always has been, and, in spite of all the regulations which can be made, always must be, a mere piece of quackery, it is certainly for the advantage of the public that it should be understood to be so. It is in a particular manner for the advantage of the Universities that, for the resort of students, they should be obliged to depend, not upon their privileges but upon their merit,—upon their abilities to teach, and their diligence in teaching; and that they should not have it in their power to use any of those quackish arts which have disgraced and degraded the half of them.

"A degree which can be conferred only upon students of a certain standing is a

statute of apprenticeship which is likely to contribute to the advancement of science, just as other statutes of apprenticeship have contributed to that of arts and manufacturers. Those statutes of apprenticeship, assisted by other corporation laws, have banished arts and manufactures from the greater part of towns-corporate. Such degrees, assisted by some other regulations of a similar tendency, have banished almost all useful and solid education from the greater part of universities. Bad work and high price have been the effect of the monopoly introduced by the former; quackery, imposture, and exorbitant fees, have been the consequences of that established by the latter. The industry of manufacturing villages has remedied in part the inconveniences which the monopolies established by towns-corporate had occasioned. The private interest of some poor Professors of Physic in some poor Universities inconveniently situated for the resort of students has in part remedied the inconveniences which would certainly have resulted from that sort of monopoly which the great and rich Universities had attempted to establish. The great and rich Universities seldom graduated anybody but their own students, and not even them till after a long and tedious standing; five and seven years for a Master of Arts; eleven and sixteen for a Doctor of Law, Physic or Divinity. The poor Universities, on account of the inconveniency of their situation, not being able to get many students, endeavoured to turn a penny in the only way in which they could turn it, and sold their degrees to whoever would buy them, generally without requiring any residence or standing, and frequently without subjecting the candidate even to a decent examination. The less trouble they gave, the more money they got, and I certainly do not pretend to vindicate so dirty a practice. All Universities being ecclesiastical establishments, under the immediate protection of the Pope, a degree from one of them gave, all over Christendom, very nearly the same privileges which a degeee from any other could have given; and the respect which is at this day paid to foreign degrees, even in Protestant countries, must be considered as a remnant of Popery. The facility of obtaining degrees, particularly in physic, from those poor Universities had two effects, both extremely advantageous to the public, but extremely disagreeable to graduates of other universities whose degrees had cost them much time and expense. *First*, it multiplied very much the number of doctors, and thereby no doubt sunk their fees, or at least hindered them from rising so very high as they otherwise would have done. Had the universities of Oxford and Cambridge been able to maintain themselves in the exclusive privilege of graduating all the doctors who could practise in England, the price of feeling a pulse might by this time have risen from two and three guineas, the price which it has now happily arrived at, to double or triple that sum; and English physicians might, and probably would have been, at the same time, the most ignorant and quackish in the world. *Secondly*, It reduced a good deal the rank and dignity of a doctor, but if the physician was a man of sense and science, it would not surely prevent his being respected and employed as a man of sense and science. If he was neither the one nor the other, indeed, his doctorship would no doubt avail him the less. But ought it in this

case to avail him at all? Had the hopeful project of the rich and great Universities succeeded, there would have been no occasion for sense or science. To have been a doctor would alone have been sufficient to give any man rank, dignity, and fortune enough. That in every profession the fortune of every individual should depend as much as possible upon his merit, and as little as possible upon his privilege, is certainly for the interest of the public. It is even for the interest of every particular profession, which can never so effectually support the general merit and real honour of the greater part of those who exercise it, as by resting on such liberal principles. Those principles are even most effectual for procuring them all the employment which the country can afford. The great success of quacks in England has been altogether owing to the real quackery of the regular physicians. Our regular physicians in Scotland have little quackery, and no quack accordingly has ever made his fortune among us.

"After all, this trade in degrees I acknowledge to be a most disgraceful trade to those who exercise it; and I am extremely sorry that it should be exercised by such respectable bodies as any of our Scotch Universities. But as it serves as a corrective of what would otherwise soon grow up to be an intolerable nuisance, the exclusive and corporation spirit of all thriving professions and of all great Universities, I deny that it is hurtful to the public.

"What the physicians of Edinburgh at present feel as a hardship is, perhaps, the real cause of their acknowledged superiority over the greater part of other physicians. The Royal College of Physicians there, you say, are obliged by their charter to grant a licence, without examination to all the graduates of Scotch Universities. You are all obliged, I suppose, in consequence of this, to consult sometimes with very unworthy brethren. You are all made to feel that you must rest no part of your dignity upon your degree, a distinction which you share with the men in the world, perhaps, whom you despise the most, but that you must found the whole of it upon your merit. Not being able to derive much consequence from the character of Doctor, you are obliged, perhaps, to attend more to your character as men, as gentlemen, and as men of letters. The unworthiness of some of your brethren may, perhaps, in this manner be in part the cause of the very eminent and superior worth of many of the rest. The very abuse which you complain of may in this manner, perhaps, be the real source of your present excellence. You are at present well, wonderfully well, and when you are so, be assured there is always some danger in attempting to be better.

"Adieu, my dear Doctor; after having delayed to write to you, I am afraid I shall *get my lug* [*ear*] *in my lufe* [*hand*], as we say, for what I have written. But I ever am most affectionately yours,

"Adam Smith.

"London, 20th September 1774."

F. W. Hurst, in his biography of Smith, says he "probably pushed his argument for free trade in medical degrees to this extreme mainly from

anxiety to prevent the interference of an unwise Government in his favorite Universities, though partly, no doubt, because he thought fraudulent competition better than none, partly again for love of maintaining a paradox."

That the government of the time was as unwise in such matters as any that England had ever had, no historian will deny. It was the same government that, less than ten years before, had rejected William Hunter's offer to found a perpetual school of Anatomy. The government was merely to furnish a piece of ground to build upon, and William Hunter was to erect the building, at a personal cost of £ 7,000, and to immediately give it over to the public with a library worth more than £3,000 and a museum of even greater value. Buckle says of George III: "Every liberal sentiment, everything approaching to reform, nay, even the mere mention of inquiry, was an abomination in the eyes of that narrow and ignorant prince."

Apparently Smith's reply convinced the leaders of Edinburgh medicine to do nothing further in this direction. During the remaining years of Cullen's life, he held fast to the views set forth in the "Memorial," but he apparently felt that it was unwise to arouse official action.

ON THE MANNER OF ANASTOMOSIS OF THE HEPATIC AND PORTAL CIRCULATIONS

JOHN McKEE OLDS AND EDWARD STEPHEN STAFFORD

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It is commonly understood that there is some form of communication in the liver between portal venous circulation and hepatic arterial circulation, but the exact nature of this communication has not been fully demonstrated. The present study was undertaken in the hope of shedding some light upon this question, because the solution to many pathological and physiological problems (typical intralobular localization of various necroses, volume control, pressure relations, reservoir action, and so on) may depend upon a more exact knowledge of the hepatic circulation. It was felt that an injection method would inevitably provide a clear demonstration of the characteristics of the vascular distribution.

In reviewing the literature we found that the research of Mall ('06) was the earliest work upon the details of liver circulation of any importance to this study, other than historical. Mall considered the portal unit as the true structural unit of the liver. He recognized, as we do today, three possibilities for the terminal distribution of the hepatic artery: first, direct arterio-venous connections without capillaries (arterio-venous fistulae); second, an interposed capillary bed between portal vein and hepatic artery outside the lobule, the so-called "internal roots" to the portal vein; and lastly, intercommunication of the vascular beds within the hepatic lobule. After examination of hundreds of injection-preparations, he stated that he had never seen either the first or second type, but that the long, delicate hepatic arteries gave rise to capillary plexuses about the bile-ducts, and then entered the center of the portal units together with a terminal portal twig, and finally communicated with the capillaries of the lobule. He did not describe the actual junctions, however. His studies were in large part concerned with the number and size of the various orders of branches of the portal vein and hepatic artery and vein, and their

relative distribution. However, he did state that by far the greater number of arteries entered the portal units, breaking up at once into capillaries destined to supply the periphery of the lobules. Further, he pointed out that the great bulk of arterial blood was equally distributed from the centers of the portal units and was fully mixed with portal blood before it reached the hepatic veins. On the other hand, he made no mention of pressure relations.

At about that same time, Gilbert and Villaret ('09), in France, investigated the circulation of the liver by similar injection methods. Their work, which was excellent, seems to have been lost sight of. They made single injections of the various vascular components of the liver, and, judging by their illustrations, their results were similar to those of Mall. Apparently they were not familiar with Mall's work, and their conclusions were more physiological than anatomical. But they, too, concluded that most of the arterial blood entered the lobule directly, and not indirectly by means of the so-called "inner roots" to the portal vein in the interlobular spaces. Moreover, they never secured complete injections of the lobules,—an observation that led them to conclude that the liver tissue exerted some "vital reaction," by which they meant a power on the part of the living walls of the intralobular blood spaces to contract and thus propel blood. They did not, however, carry their anatomical investigation to the point of demonstrating the actual junction of the hepatic and portal systems. Finally, they did not consider the hepatic sinusoids to be everywhere anastomosing, but thought that the capillary beds of the hepatic artery and portal vein constituted independent capillary systems, each communicating separately with the hepatic vein.

Burton-Opitz ('10) studied the vascularity of the liver from a physiological standpoint only. Winternitz ('11), in his studies on the effect upon the liver of occlusion of the various hepatic vessels, thought that the portal vein supplied the acini, while the hepatic artery supplied the interlobular tissue and joined the portal vein in the interlobular spaces. MacLeod and Pearce ('14), studying the volume relations of fluids passing through the vascular bed of the liver, make no mention of the morphology of the arterio-venous junctions. Pfuhl ('21) made a reconstruction of the liver lobule of the pig, but did not describe the termination of the hepatic artery. In a later paper ('22), describ-

ing a reconstruction of the human liver lobule, he wrote: "The arteries furnish blood supply for the interlobular spaces and the walls of the hepatic veins. They also send capillaries between the lobules, which communicate with perilobular capillaries." Loeffler ('27) believed that the hepatic artery capillaries never communicated directly with sinusoids but supplied the bile-ducts and portal spaces, and anastomosed by means of a capillary bed in the portal spaces with the portal veins, *i.e.*, the internal roots of the portal vein, or perilobular capillaries.

McIndoe ('28), in a study of the vascular lesions of portal cirrhosis by a corrosion method, concluded that the hepatic artery communicated both with the portal vein and hepatic sinusoids.

Braus ('24) described a translobular artery, which directly traversed the liver lobule, nourishing the tissue about the central veins, but his pictures of reconstructions of the liver lobule do not portray the ultimate breaking up of the hepatic artery.

In summary, then, we have the following views: The early workers —Mall, Gilbert and Villaret—from experimental evidence believed in direct union of the branches of the portal vein and the hepatic artery at the periphery of the lobule. The later anatomists, especially Pfuhl and Loeffler, adhered to the view that portal-hepatic arterial communication was indirect, occurring in the portal space by means of an interposed interlobular capillary bed. In support of this view they did not present adequate experimental observations. As a consequence of these conflicting views there exists, up to the present time, great uncertainty and confusion in regard to the exact manner and point of junction of the hepatic arterial and portal venous circulation within the liver lobule. It is the purpose of this study to reinvestigate the controversial subject of direct or indirect communication, and to elucidate the exact mode and site of junction between the portal venous and the hepatic arterial trees.

METHODS AND MATERIAL

The method consisted in the injection of two contrasting masses, fluid enough to flow through the smallest capillaries and yet of enough body to fill the larger sinuses and vessels. The injection fluids were tried out first in a single injection method, for which cats were used.

The cat was etherized, the thoracic and abdominal cavities opened, a scissors-snip made in the right ventricle, and the animal bled to death. The thoracic aorta was cannulated, and ligated above the cannula, and below the coeliac axis. Moreover, the portal vein was ligated. Warm physiological saline was then injected until the outflow from the right ventricle was nearly colorless. In several animals, a two per cent. suspension of Prussian blue in distilled water was injected, according to the technique of Hinman ('23), but this substance was found to be unsatisfactory for good injections of the liver. In a second series, a one-to-one suspension of Higgins' Waterproof India Ink in distilled water, to which a few drops of concentrated ammonium hydroxide were added, was used. These injections proved to be excellent. Various pressures were tried. Injecting at 120 mm. of mercury, the hepatic arterial capillaries did not become entirely filled, even when the pressure was maintained for an hour. But with much higher pressure, it was possible to obtain good complete injections in a few moments. The completion of the injection was judged by the amount of the outflow from the right ventricle, and the appearance of the vessels of Glisson's capsule. Following injection, the hepatic artery and the inferior vena cava were ligated, and the whole liver was removed and fixed immediately in ten per cent. formalin.

For the double injections India ink and carmine gelatin were found to be most advantageous. Ranvier's carmine gelatin was prepared according to the technique of Lee ('24). India ink was injected into the hepatic artery, carmine gelatin into the portal vein. Cats were prepared as before, excepting that the portal vein was cannulated as well. The best portal venous injections were obtained at pressures greater than 40 mm. of mercury.

The manner of anastomosis of the venous and arterial vascular beds was studied in human livers as well as in those of cats. Fresh autopsy material was very kindly furnished by the Department of Pathology. Livers were selected from cases, autopsied very shortly after death, in which there had been no clinical evidence of any liver disease. The livers were removed *in toto* from the cadaver as quickly and carefully as possible. They were immediately placed in warm saline, and the portal vein and hepatic artery cannulated. An injection of warm saline was instituted until the outflow from the hepatic veins

was nearly colorless. Following this the double injection was made. The injection was stopped when both masses flowed freely from the hepatic veins, and when the capsule appeared well injected. The portal vein, hepatic artery, and the hepatic veins were at once ligated and the whole liver was fixed in 10-per-cent. formalin. Four to six hours later the liver was cut into slices (about 1 to 2 cm. thick) and placed in fresh formalin, for more adequate fixation.

Completely injected areas were selected to be cut serially at 40μ. A light stain with haematoxylin or carmalum gave the best contrast to both masses.

OBSERVATIONS AND DISCUSSION

In our first injections, made at low pressure, we found that the masses had penetrated only the peripheral zone of the lobules. Similarly, when injected at high pressure, but without immediate ligation of the hepatic veins upon completion of the injection, the masses had again filled only the periphery of the lobules. The explanation of both of these results is simple: the liver, when its large vessels are opened, collapses immediately. To overcome this collapsed state considerable pressure must be used on injection. While the excised liver is being injected it swells greatly, and finally reaches a point where the output from the hepatic veins equals the input of the injection. If the injection pressure is withdrawn, the liver again collapses at once, the collapse being accompanied by the escape of the injection masses from the hepatic veins. The lobules, if examined now, are found to have been drained of injection mass about the central veins, only the injection of the periphery remaining. Gilbert and Villaret ascribed this phenomenon of emptying to a "vital reaction" on the part of the liver tissue. On the other hand, we believe that it is natural that the wide hepatic sinusoids should tend to collapse, since, as is well known, there is a remarkable absence of rigid supporting framework within the lobules, whereas the capsule of Glisson contains a great quantity of elastic tissue fibers. This collapse is probably prevented in the normal living body by several factors: first, the constant inflow of blood under pressure and, second, the existence of a certain amount of back pressure in the hepatic veins. In the injected specimen we can prevent collapse by ligating all of the vessels at the time of with-

drawing the injection pressure, thereby securing a completely distended vascular bed within each lobule.

The liver lobule, doubly injected by the present method, has yielded a constant and characteristic picture. Commencing at a large portal space, or so-called interlobular nodal point, there is a portal venule, and at least one hepatic arteriole. The portal venule is seen to give off small branches which divide into twigs coursing towards the periphery of the portal space. At the boundaries of the lobules each of these twigs enters the hepatic sinusoids.

The hepatic arteriole gives off branches that are smaller than the corresponding branches of the portal venules. These branches of the hepatic arterioles break up into capillaries supplying the portal space. In the neighborhood of the biliary passages these capillaries form plexuses around the bile-ducts. They also form the vasa vasorum of the walls of the portal vessels.

The hepatic arterial capillaries never anastomose directly with the portal vein radicals within the portal spaces. Instead, the arterial capillaries enter the hepatic sinusoids independently of the venous anastomoses. Slender capillaries arise either as the ultimate radicals of finer branches of the hepatic artery, or as offshoots from the capillary plexuses surrounding the bile-ducts. These capillary branches course towards the periphery of the portal space and anastomose with the hepatic sinusoids. The junctions of the arterial capillaries with the sinusoids are always independent of, and at some distance from, the similar communications established by the veins. Hence the most peripheral sinusoids are initially either distinctly arterial or venous, as the case may be. The venous connections are more numerous, approximately four or five venules communicating with the sinusoids of a lobule to one arterial connection. Striking is the disparity in size of the venules and arterial capillaries at their points of anastomosis with the sinusoids. The venules are slightly larger or at least of the same caliber as the sinusoids which they enter, so that relatively open communications exist. The arterial capillaries, on the other hand, are relatively long and slender, so that at the points of communication with the sinusoids the caliber of the vascular bed widens out abruptly. The blood passes in this instance from a conducting system of narrow diameter into one which is several times as wide in caliber. The

relationships which have been described, of the arterial and venous radicals to the sinusoids, are illustrated in Figures 1 and 2.

MacLeod and Pearce ('14) postulated the equality of pressure of the arterial and venous blood-streams in the periphery of the lobule. The anatomical character of the junction of the arterial twigs with the sinusoids justifies the belief that the reduction in pressure from the

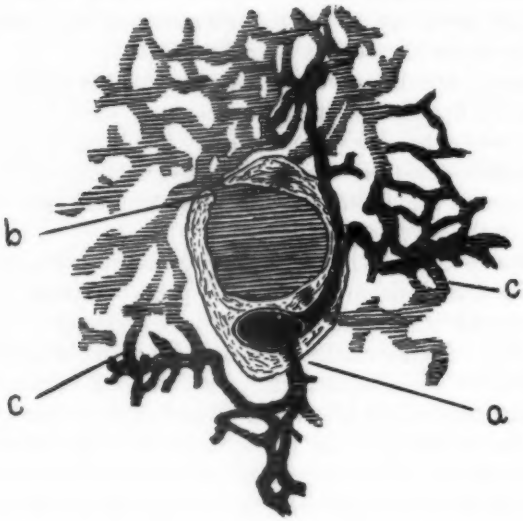

FIG. 1. A CROSS-SECTION OF AN INTERLOBULAR NODAL POINT IS SHOWN

For the sake of clarity the bile-duct has not been represented. Note the distribution of the hepatic arteriole (*a*), that of the portal venule (*b*), and the intersinusoidal communications (*c*).

Figs. 1 and 2 are camera lucida drawings from actual fields.

arterial to the hepatic level is accomplished by a decrease in resistance attributable to the abrupt widening of the vascular bed at the points where the hepatic capillaries join the sinusoids.

The arterial and portal twigs have been traced to their ultimate communications with the hepatic sinusoids at the periphery of a lobule. The lobule is composed of a labyrinth of cells which are arranged in columns separated by anastomosing sinusoids. At the periphery of

the lobule, there is a short length of sinusoid which is characteristically filled by either arterial or venous blood, but not by both. Hence the

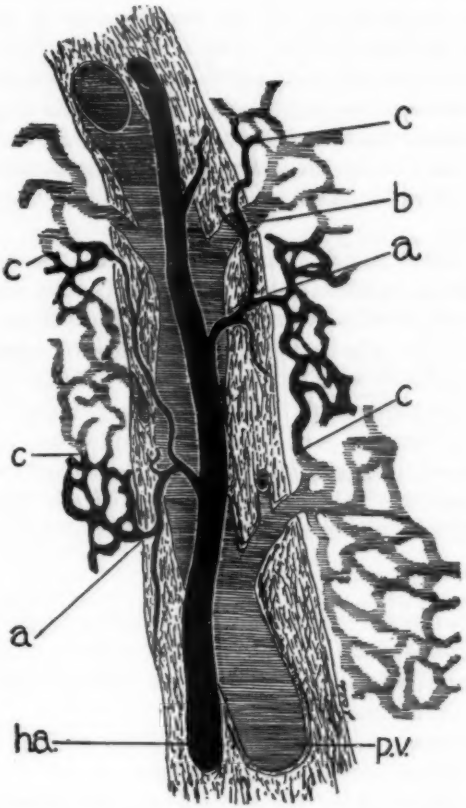

FIG. 2. A LONGITUDINAL-SECTION THROUGH AN INTERLOBULAR OR PORTAL SPACE IS SHOWN

Note the distribution of hepatic arterioles (*a*), portal venules (*b*), and the intersinusoidal communications. The abrupt transition from narrow arterial channel to wide sinusoidal channels is illustrated. Note the mixing of the two injection masses at level of first sinusoidal anastomosis and thereafter.

initial segments of the sinusoids at the periphery of the lobule are filled solely, as the case may be, with venous or with arterial blood.

Obviously the two bloods will not mix before reaching the first anastomotic junction of the sinusoids. The exact point of intermingling is distant three to seven cell-diameters from the periphery of the liver lobule. The intermingling of the two streams is probably not completed at the first junction. Contributory to rapid mixing, however, is the fact that the courses of these sinusoids are very tortuous, and the anastomoses in every direction are extremely frequent. Two conclusions appear warranted: first, there can be no mixing of portal and arterial blood before the first sinusoidal anastomosis, and second, mixing must be accomplished in a very short distance beyond the first anastomosis.

We have looked through our material in vain for any capillaries in the interlobular spaces which communicate directly with the portal veins. The only capillaries seen are the arterial capillaries of Glisson's capsule and of the bile-duct plexuses, the direct communication of which with the lobule we have already traced. We have also failed to substantiate the presence of the translobular arteries of Braus. With regard to these latter, it is possible sometimes to find a field in which there is a vessel resembling that of Braus, but when the next serial section is examined, it is seen at once that this is merely a vessel coursing longitudinally along the edge of the interlobular space.

CONCLUSIONS

1. The hepatic artery communicates by means of capillaries directly with the sinusoids of the liver lobule at the periphery of the lobule.

2. The portal vein also communicates directly with the hepatic sinusoids at the periphery of the lobule.

3. On the contrary, there are no interlobular capillary anastomoses between the hepatic artery and portal vein.

4. The capillaries of the bile-duct plexuses (branches of the hepatic artery) communicate directly with the hepatic sinusoids at the periphery of the lobule.

5. No translobular arteries can be demonstrated.

6. Mixing of hepatic arterial and portal venous blood occurs via the outermost or peripheral sinusoidal anastomoses, but not within the interlobular tissue itself.

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EXPERIENCES WITH ARTIFICIAL HELIOTHERAPY[1]

(An Abstract)

HENRY STUART WILLIS

Within comparatively recent years heliotherapy in medicine has reached the proportions of a fad and has become a panacea among laymen and many physicians. It has been applied in almost every disease, mostly without criteria or control. That it is a valuable therapeutic agent in some pathological conditions cannot be gainsaid, but that it is helpful for the wide array of clinical disorders in which it is uncritically applied, is certainly to be questioned.

The absence of reasonable proof of the therapeutic efficacy of ultraviolet light therapy in most diseases seemed sufficient justification for using the light treatment clinic as an experimental station in which every alternate patient would be exposed to the light and every other one deprived of it. This was done by placing a piece of plate glass under one of the two lights in the clinic. Such matters as the rate of deterioration of the lamps, distance from lamp to patient, psychic influence upon the patient, general management of the patient, etc., as well as the distribution of colored and white patients, were all kept as nearly constant as possible in the two groups. Exposures were *general*, were made three times a week, reached an average maximum of forty minutes front and back, and extended over a period of about six months.

A small group of ninety-four patients has been studied to date. The types of disease varied rather widely. Adenitis, mostly tuberculous, was the most frequent diagnosis. Numerous cases of tuberculosis of the tracheobronchial lymph nodes, of the skin (erythema induratum), peritoneum and genito-urinary system were treated. Chronic arthritis, chronic infectious arthritis and osteomyelitis were all represented in fair numbers. A few cases of secondary anaemia, post-operative convalescence, etc., completed the list.

The cases came chiefly from the surgical, orthopedic and medical clinics. Each patient was given a complete physical examination and an x-ray examination of the chest and each was reëxamined approximately every month in both the originating and the medical clinic, of which latter the light clinic is a part.

There is an obvious danger in coming to hard and fast deductions from such a comparatively small number of cases, and this possibility has been borne in mind with the result that the cases have been classified simply as "improved" or "unimproved" in the two groups. It is obvious that in considering results we must regard both general and local, and both subjective and objective changes.

With these criteria in mind the following results were obtained. These are represented in chart form for the sake of clearness and brevity.

All cases

Total number of patients treated in U. V. L. group	91
Total number in control group	47
Total number in series	138
Cases insufficiently treated	44
Cases under discussion	94

[1] Presented before the Research Society, Johns Hopkins Hospital, April 4, 1930.

Results—All cases

Total number of cases..... 94
Treated..... 64
Controls..... 30

Treated		*Controls*	
Improved	35 = 54.5%	Improved	17 = 56.66%
Unimproved	29 = 45.5%	Unimproved	13 = 43.33%

Results—Cases of adenitis

Total number of cases..... 37
Treated..... 28
Controls..... 9

Treated		*Controls*	
Improved	19 = 68%	Improved	5 = 55.5%
Unimproved	9 = 32%	Unimproved	4 = 44.5%

It is clear from these data that the ultraviolet light conferred no material benefit on the general run of patients—or at least that the percentage of improvement was practically the same in the two groups. However, the following statements are justifiable.

In the first place the treated group of patients with *adenitis* (mostly tuberculous) showed improvement in general. Several individuals of this group showed a remarkable degree of improvement. This was particularly true in those who had a sinus tract.

Secondly: A large percentage of the treated patients experienced a definite tonic effect in the way of subjective well-being, improvement in appetite and increase in weight. This was not a feature in the control group.

Thirdly: Pigmentation seemed to depend upon the size of the initial or early doses and the rate of increase of exposure (*i.e.*, on the degree of erythema). It appeared to have nothing to do with the degree of improvement or lack of improvement. There was no material difference in response among white and colored people. .

Fourthly: Plate glass screens out the short ultraviolet light waves—those which produce pigmentation and those which are specific in preventing and curing rickets—but it transmits the longer ultraviolet waves, the visible waves and some of the infra-red waves. The effect of these waves upon disease is entirely unknown and should be studied. It is planned to run a third group of control patients who do not get these waves.

Finally: It should be noted that these are impressions only, and not conclusions, that the few cases studied do not represent a cross-section of disease as it is seen in our dispensaries and that much more must yet be done on the question before definite conclusions are forthcoming. We have not studied many of the cutaneous diseases, granulating wounds, etc., which are said to respond favorably to ultraviolet light treatment.